UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

DAIICHI SANKYO CO., LTD., 3-5-1, Nihonbashi Honcho, Chuo-Ku Tokyo, Japan 203-8426 PLAINTIFF, v. HON. DAVID J. KAPPOS UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY AND DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE Office of General Counsel Madison West Building 600 Dulany Street, Room 10B20 Alexandria, VA 22313-1450, DEFENDANT	**CASE NUMBER**

COMPLAINT

Plaintiff Daiichi Sankyo Co., Ltd. ("Daiichi Sankyo") for its Complaint against the Honorable David J. Kappos, hereby alleges as follows:

NATURE OF THE ACTION

1. This is an action by the assignee of United States Patent No. 7,935,835 ("the '835 Patent") seeking judgment, pursuant to 35 U.S.C. § 154(b)(4)(A), that the patent term adjustment for the '835 Patent be changed from 55 days to 57 days.

2. This action arises under 35 U.S.C. § 154 and the Administrative Procedure Act, 5 U.S.C. §§ 701-706.

THE PARTIES

3. Plaintiff Daiichi Sankyo is a corporation organized and existing under the laws of Japan, having a principal place of business at 3-5-1, Nihonbashi Honcho, Chuo-Ku, Tokyo, Japan, 203-8426.

4. Defendant Honorable David J. Kappos (hereinafter "Director") is the Under Secretary of Commerce for Intellectual Property and Director of the U.S. Patent and Trademark Office ("PTO"), acting in his official capacity. The Director is the head of the PTO, charged by statute with providing management supervision for the PTO and for the issuance of patents. The Director is the official responsible for determining the period of patent term adjustment under 35 U.S.C. § 154.

JURISDICTION AND VENUE

5. This Court has jurisdiction to hear this action and is authorized to issue the relief sought pursuant to 28 U.S.C.§§ 1331, 1338(a), and 1361, 35 U.S.C.§ 154(b)(4)(A) and 5 U.S.C. §§ 701-706.

6. Venue is proper in this district by virtue of 35 U.S.C. § 154(b)(4)(A).

7. This Complaint is timely filed in accordance with 35 U.S.C. § 154(b)(4)(A).

FACTUAL BACKGROUND

8. Tomio Kimura, Nobuyuki Ohkawa, Takayoshi Nagasaki, Atsuhiro Sugidachi, and Osamu Ando are the inventors of the invention claimed in United States Patent Application No. 12/066,813 ("the '813 application") entitled "Substituted Cycloalkene Derivative," which issued as the '835 Patent on May 3, 2011. The '835 patent is directed to compounds to suppress intracellular signal transduction or cell activation induced by endotoxin. The '835 Patent is attached hereto as Exhibit A.

9. Plaintiff Daiichi Sankyo is the assignee of the '835 patent, as evidenced by the assignment document recorded at the PTO. Daiichi Sankyo is therefore the real party in interest

in this case.

10. Section 154 of Title 35 of the United States Code requires that the Director of the PTO grant a patent term adjustment in accordance with the provisions of Section 154(b). Specifically, 35 U.S.C. § 154(b)(3)(D) states that "[t]he Director shall proceed to grant the patent after completion of the Director's determination of a patent term adjustment under the procedures established under this subsection, notwithstanding any appeal taken by the applicant of such determination."

11. In determining patent term adjustment, the Director is required to extend the term of a patent for a period equal to the total number of days attributable to delay by the PTO under 35 U.S.C. § 154(b)(1), as limited by any overlapping periods of delay by the PTO as specified under 35 U.S.C. § 154(b)(2)(A), any disclaimer of patent term by the applicant under 35 U.S.C. § 154(b)(2)(B), and any delay attributable to the applicant under 35 U.S.C. § 154(b)(2)(C).

12. The '813 application was filed on September 13, 2006, and issued as the '835 Patent on May 3, 2011.

13. The Director made a determination of patent term adjustment pursuant to 35 U.S.C. § 154(b)(3) of 55 days and issued the '835 Patent reflecting that determination on the face of the patent. (*See* Ex. A at 1).

14. Section 154(b)(4)(A) of Title 35 of the United States Code provides that "[a]n applicant dissatisfied with a determination made by the Director under paragraph (3) shall have remedy by a civil action against the Director filed in the United States District Court for the District of Columbia within 180 days after grant of the patent. Chapter 7 of Title 5 shall apply to such an action."

CLAIM FOR RELIEF

15. The allegations of paragraphs 1-14 are incorporated into this claim for relief as if fully set forth herein.

16. Pursuant to 35 U.S.C. § 154(b)(4)(A), Daiichi Sankyo seeks relief from the Director's erroneous determination of the 55-day patent term adjustment period for the '835 Patent.

17. The Director erroneously determined that Daiichi Sankyo was responsible for two days of delay pursuant to 35 U.S.C. § 154(b)(2)(C), when in fact, there was no applicant delay pursuant to 35 U.S.C. § 154(b)(2)(C). The correct patent term adjustment for the '835 Patent is 57 days.

17. Under 35 U.S.C. § 154(b)(1)(A), the total number of days attributable to PTO examination delay ("A delay") is 7 days.

18. Under 35 U.S.C. § 154(b)(1)(B), the number of days attributable to the PTO's failure to issue the '835 Patent within three years of application pendency ("B Delay") is 50 days.

19. Under 35 U.S.C. § 154(b)(2)(A), the total number of days constituting an overlap of A Delay and B Delay is zero days.

20. Under 35 U.S.C. § 154(b)(2)(C), the total period of PTO delay is to be reduced by the period of applicant delay. The Director determined the period of applicant delay for the '835 Patent was two days because a reply to an June 25, 2010 office action was filed on September 27, 2010, three months and two days after the office action was mailed. The Director based his calculation on 35 U.S.C. § 154(b)(2)(C)(ii), which states that "an applicant shall be deemed to have failed to engage in reasonable efforts to conclude processing or examination of an application for the cumulative total of any periods of time in excess of 3 months that are taken to respond to a notice from the Office making any rejection."

21. The Director's determination that there were two days of applicant delay was erroneous for the following reasons. The date which was three months from the mailing of the office action was September 25, 2010 – a Saturday on which the PTO was closed. Although 35 U.S.C. § 154(b)(2)(C)(ii) sets forth a three month period for filing a response to a notice from the PTO making any rejection, that section must be read in conjunction with 35 U.S.C. § 21(b),

which mandates that if the last day of a statutory period for taking any action falls on a Saturday, Sunday, or a Federal holiday, the action may be taken on the next succeeding secular or business day. The three month statutory period for filing a response was extended, by operation of 35 U.S.C. § 21(b), to the next business day, and a response filed on the next business day after September 25, 2010 should have been deemed to be a timely response.

22. Daiichi Sankyo submitted the response on the business day following September 25, 2010, a Saturday on which the PTO was closed for business. Daiichi Sankyo's filing of a response to the office action on September 27, 2010 cannot be deemed to be "applicant delay" or a failure "to engage in reasonable efforts to conclude processing or examination of an application" when it was in fact *a timely response* for the three month period set for response to the office action.

23. Accordingly, the correct patent term adjustment should be calculated as follows: 7 days (A Delay) + 50 days (B Delay) - 0 days (overlap) - 0 day (applicant delay) = 57 days.

24. The Director erred in the determination of patent term adjustment for the '835 Patent by erroneously attributing two days of applicant delay when there were no days of applicant delay. Thus, the Director incorrectly determined that the net patent term adjustment for the '835 Patent was 55 days. The Director has deprived Daiichi Sankyo of the full patent term adjustment to which it is entitled, which is 57 days.

25. The Director's determination that the '835 Patent is entitled to 55 days of patent term adjustment instead of 57 days of patent term adjustment is arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law and in excess of statutory jurisdiction, authority, or limitation.

PRAYER FOR RELIEF

Wherefore, Daiichi Sankyo demands judgment against Defendant and respectfully requests that this Court:

a. Enter judgment in favor of Daiichi Sankyo;

b. Enter an order changing the period of patent term adjustment for the '835 Patent term from 55 days to 57 days;

c. Order the Director to extend the term of the '835 Patent to reflect the 57 day patent term adjustment; and

b. Grant such other and future relief as the nature of the case may admit or require and as may be just and equitable.

Dated: October 25, 2011

Respectfully submitted,

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EXHIBIT A

US007935835B2

(12) **United States Patent**
Kimura et al.

(10) **Patent No.: US 7,935,835 B2**
(45) **Date of Patent: May 3, 2011**

(54) **SUBSTITUTED CYCLOALKENE DERIVATIVE**

(75) Inventors: **Tomio Kimura**, Tokyo (JP); **Nobuyuki Ohkawa**, Tokyo (JP); **Takayoshi Nagasaki**, Tokyo (JP); **Atsuhiro Sugidachi**, Tokyo (JP); **Osamu Ando**, Tokyo (JP)

(73) Assignee: **Daiichi Sankyo Company, Limited**, Tokyo (JP)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 55 days.

(21) Appl. No.: **12/066,813**

(22) PCT Filed: **Sep. 13, 2006**

(86) PCT No.: **PCT/JP2006/318103**

§ 371 (c)(1),
(2), (4) Date: **Jan. 8, 2009**

(87) PCT Pub. No.: **WO2007/032362**

PCT Pub. Date: **Mar. 22, 2007**

(65) **Prior Publication Data**

US 2009/0233952 A1 Sep. 17, 2009

(30) **Foreign Application Priority Data**

Sep. 14, 2005 (JP) 2005-267504

(51) **Int. Cl.**
C07D 319/00 (2006.01)
C07D 315/00 (2006.01)
C07D 327/00 (2006.01)

(52) **U.S. Cl.** **549/332**; 333/336; 333/337; 333/338; 333/341; 333/14; 333/20; 333/22

(58) **Field of Classification Search** 549/332, 549/333, 336, 337, 338, 341, 14, 20, 22
See application file for complete search history.

(56) **References Cited**

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FOREIGN PATENT DOCUMENTS

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JP	2004-002370 A	1/2004
WO	0041698 A1	7/2000

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Beutler, "Inferences, questions and possibilities in Toll-like receptor sinalling", Nature, Jul. 8, 2004, vol. 430, pp. 257-263.

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Cook, Donald N. et al., "Toll-like receptors in the pathogenesus of human disease", Nature Immunology, Oct. 2004, vol. 5, No. 10, pp. 975-979.

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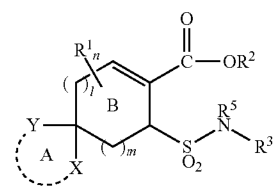
Primary Examiner — Janet L. Andres
Assistant Examiner — Raymond Covington
(74) *Attorney, Agent, or Firm* — Dorsey & Whitney LLP

(57) **ABSTRACT**

A compound of formula (I)

(I)



Wherein X, Y, ring A, ring B, l, m, R^1, R^2, R^4 and R^5 are as defined herein, to supress intracellular signal transduction or cell activation induced by endotoxin and to suppress cell responses due to the intracellular signal transduction and cell activation such as an excess generation of inflammatory mediators such as TNF-α, pharmacologically acceptable salts therefor, a preparation method therefor, and a medicament containing the aforementioned substituted cycloalkene derivative as an active ingredient which is superior in prophylaxis and/or treatment of diseases such as sepsis (septic shock, disseminated intravascular coagulation, multiple organ failure and the like), that are associated with intracellular signal transduction or cell activation induced by endotoxin and to cell responses to the intracellular signal transduction and cell activation.

45 Claims, No Drawings

SUBSTITUTED CYCLOALKENE DERIVATIVE

CROSS-REFERENCE TO RELATED APPLICATION

This Application is a Section 371 National Stage Application of International Application No. PCT/JP2006/318103, filed 13 Sep. 2006 and published as WO 2007/032362 A1 on 22 Mar. 2007, which claims the priority from the Japanese application 2005-267504, filed 14 Sep. 2005, the subject matter of which are hereby incorporated by reference in its entirety.

TECHNICAL FIELD

The present invention relates to a novel compound which has an action to suppress intracellular signal transduction or cell activation in various cells such as monocytes, macrophages and vascular endothelial cells, the intracellular signal transduction or cell activation being induced by endotoxin, and to suppress the generation of inflammatory mediators such as TNF-α due to the intracellular signal transduction and cell activation, and which is useful as a prophylactic and/or therapeutic agent for various diseases such as sepsis (septic shock, disseminated intravascular coagulation, multiple organ failure and the like), a production method therefor and a use thereof.

BACKGROUND ART

Sepsis is a systemic inflammatory response syndrome (SIRS) which occurs due to an excess inflammatory response of a biological body against bacterial infection, and is a disease which may result in death when it is accompanied by shock or organ failure. Since there are only a few agents that are effective against sepsis until now, it is considered to be a disease that is difficult to prevent and treat. However, since its fatality is high and the number of patients is large, development of therapeutic agents for it is particularly important (for example, refer to Non-patent document 1).

Endotoxin (lipopolysaccharide, LPS), which is a membrane component of bacteria, acts against cells such as monocytes, macrophages and vascular endothelial cells, induces an excess generation of various inflammatory mediators such as TNF-α and the like, causes sudden blood pressure reduction, blood coagulation disorders, cardiovascular disturbances and the like in addition to systemic inflammatory responses, and thus exhibits sepsis (for example, refer to Non-patent document 2). Lipid A, which corresponds to lipopolysaccharide and its partial structure, activates intracellular signal transduction via TLR4 (Toll-like receptor 4), which is a functional cell surface receptor, after binding with CD14 (for example, refer to Non-patent document 3). Accordingly, lipid A initiates various cell responses represented by the generation of inflammatory mediators. Therefore, it is considered that a substance which suppresses the intracellular signal transduction or cell activation induced by endotoxin, and various cell responses induced by intracellular signal transduction and cell activation, the various cell responses being represented by an excess generation of inflammatory mediators such as TNF-α, can be an effective prophylactic and therapeutic agent for sepsis (for example, refer to Non-patent document 3, Non-patent document 4, Patent document 1 and Patent document 2).

Intracellular signal transduction or cell activation induced by endotoxin, and various cell responses induced by the intracellular signal transduction and cell activation, the various cell responses being represented by an excess generation of inflammatory mediators such as TNF-α, lead to development and progress of various diseases such as ischemic brain disorder, arteriosclerosis, poor prognosis after coronary angioplasty, heart failure, diabetes, diabetic complication, joint inflammation, osteoporosis, osteopenia, autoimmune disease, tissue disorder and rejection after organ transplantation, bacterial infection, virus infection, gastritis, pancreatitis, nephritis, pneumonia, hepatitis and leukemia, in addition to the aforementioned sepsis (for example, Non-patent document 5 and Patent document 3).

Therefore, a substance which suppresses intracellular signal transduction or cell activation induced by endotoxin, and various cell responses induced by the intracellular signal transduction and cell activation such as an excess generation of inflammatory mediators such as TNF-α, is considered to be effective as a prophylactic and/or therapeutic agent for these various diseases, and thus the development of an excellent therapeutic agent has been desired.

[Non-patent Document 1] Iqbal et al., Expert Opin. Emerging Drugs, Vol. 7, page 111, 2002
[Non-patent Document 2] Hawkins et al., Current Topics in Medicinal Chemistry, Vol. 4, page 1147, 2004
[Non-patent Document 3] Beutler, Nature, Vol. 430, pages 257-263, 2004
[Non-patent Document 4] Kakutani et al., Inflammation Research, Vol. 48, page 461, 1999
[Non-patent Document 5] Donald N. Cook et al., Nature Immunology, Vol. 5, pages 975-979, 2004
[Patent Document 1] Japanese Patent Application (Kokai) No. 2000-178246
[Patent Document 2] Japanese Patent Application (Kokai) No. 2004-2370
[Patent Document 3] International Publication WO 00/41698 Pamphlet

DISCLOSURE OF THE INVENTION

Problems to be Solved by the Invention

As a result of conducting extensive studies on the pharmacological activity of various substituted cycloalkene derivatives for the purpose of developing a compound which has an activity to suppress intracellular signal transduction or cell activation in various cells such as monocytes, macrophages and vascular endothelial cells, the intracellular signal transduction or the cell activation being induced by endotoxin, and to suppress various cell responses induced by the intracellular signal transduction and cell activation, such as an excess generation of inflammatory mediators such as TNF-α, the inventors of the present invention found that a substituted cycloalkene derivative having a unique structure possesses an excellent suppressing effect against intracellular signal transduction or cell activation induced by endotoxin, and against cell responses induced by the intracellular signal transduction and cell activation, such as an excess generation of inflammatory mediators such as TNF-α, and found that it is useful as a prophylactic and/or therapeutic agent for various diseases such as sepsis which are associated with intracellular signal transduction or cell activation induced by endotoxin, and with cell responses induced by the intracellular signal transduction and the cell activation, thereby leading to completion of the present invention.

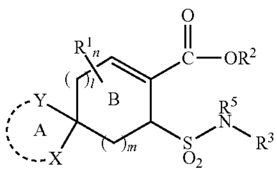
The present invention provides a substituted cycloalkene derivative which possesses an activity to suppress intracellular signal transduction or cell activation induced by endot-

oxin, and cell responses due to the intracellular signal transduction and cell activation such as an excess generation of inflammatory mediators such as TNF-α, pharmacologically acceptable salts thereof, a production method therefor, and a medicament containing the aforementioned substituted cycloalkene derivative as an active ingredient, which is excellent for prophylaxis and/or treatment of various diseases caused by intracellular signal transduction or cell activation induced by endotoxin, and caused by cell responses including an excess generation of inflammatory mediators such as TNF-α, the cell responses being induced by the intracellular signal transduction and cell activation.

Means for Solving the Problems

Accordingly, the present invention provides:

(1) A compound represented by the general formula (I):



(I)

{wherein

X and Y represent a group in which X and Y together with the carbon atom of ring B to which they are bound form ring A, X and Y together represent a substituent of ring B, or X and Y each represents a hydrogen atom.

1) In the case where X and Y represent a group in which X and Y together with the carbon atom of ring B to which they are bound form ring A:

ring A represents

a 3- to 7-membered heterocyclyl ring [in the heterocyclyl ring, X and Y, independently from each other, represent any one selected from a carbon atom, a group having the formula NR (R represents a hydrogen atom or a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_1-C_6 alkanoyl group which may be substituted with a group selected from Substituent group α), an oxygen atom, a sulfur atom, a group having the formula SO and a group having the formula SO_2,

the heterocyclyl ring may include an unsaturated bond, may form a fused ring or spiro ring with a 3- to 7-membered heterocyclyl ring or 3- to 7-membered cycloalkyl ring, and ring A, including the fused ring or spiro ring, may be substituted with the same or different 1 to 4 groups selected from the group consisting of an oxo group, a thioxo group, Substituent group α, a cyclopropyl a C_1-C_6 alkyl group,

a C_1-C_6 alkyl group which may be substituted with 1 to 5 groups selected from Substituent group α,

a C_2-C_6 alkenyl group which may be substituted with 1 to 5 groups selected from Substituent group α, and a C_2-C_6 alkynyl group which may be substituted with 1 to 5 groups selected from Substituent group α]

or

a 3- to 7-membered cycloalkyl ring (the cycloalkyl ring may include an unsaturated bond,

may form a fused ring or spiro ring with a 3- to 7-membered heterocyclyl ring or 3- to 7-membered cycloalkyl ring, and ring A, including the fused ring or spiro ring, may be substituted with the same or different 1 to 4 groups selected from the group consisting of Substituent group α, a cyclopropyl C_1-C_6 alkyl group,

a C_1-C_6 alkyl group which may be substituted with 1 to 5 groups selected from Substituent group α,

a C_2-C_6 alkenyl group which may be substituted with 1 to 5 groups selected from Substituent group α, and

a C_2-C_6 alkynyl group which may be substituted with 1 to 5 groups selected from Substituent group α).

2) In the case where X and Y together represent a substituent of ring B:

X and Y represent an oxo group or a thioxo group.

l and m, independently from each other, represent an integer of 0 to 3, and

l+m is 1 to 3.

R^1 represents

an aliphatic hydrocarbon group which may be substituted with a group selected from Substituent group β and Substituent group γ (the aliphatic hydrocarbon group represents a C_1-C_{20} alkyl group, C_3-C_{10} cycloalkyl group, C_4-C_{12} cycloalkylalkyl group, C_3-C_6 alkenyl group or C_3-C_6 alkynyl group),

a phenyl group which may be substituted with a group selected from Substituent group δ,

a group having the formula OR^4 (R^4 represents a hydrogen atom or an aliphatic hydrocarbon group which may be substituted with a group selected from Substituent group β and Substituent group γ, the aliphatic hydrocarbon group represents the same as aforementioned) or

a halogen atom.

n represents an integer of 0 to 3.

R^2 represents a hydrogen atom,

a C_1-C_6 alkyl group which may be substituted with a group selected from Substituent group β,

a C_2-C_6 alkenyl group which may be substituted with a group selected from Substituent group β, or

a C_2-C_6 alkynyl group which may be substituted with a group selected from Substituent group β.

R^3 represents

a phenyl group which may be substituted with a group selected from Substituent group ϵ, or

a 5- or 6-membered heteroaryl group which may be substituted with a group selected from Substituent group ϵ (the heteroaryl group includes 1 to 3 hetero atoms selected from a nitrogen atom, oxygen atom and sulfur atom).

R^5 represents a hydrogen atom,

a C_1-C_6 alkyl group which may be substituted with a group selected from Substituent group β,

a C_2-C_6 alkenyl group which may be substituted with a group selected from Substituent group β, or

a C_2-C_6 alkynyl group which may be substituted with a group selected from Substituent group β.

Provided that in the case where R^3 is a phenyl group which may be substituted with a group selected from Substituent group ϵ, X and Y represent the aforementioned (1) or (2).

Substituent group α represents

a hydroxy group, halogen atom, C_1-C_6 alkoxy group, halogeno C_1-C_6 alkoxy group, carboxy group, C_1-C_6 alkoxycarbonyl group;

carbamoyl group which may be substituted with a group selected from a C_1-C_6 alkyl group, C_2-C_6 alkenyl group, C_2-C_6 alkynyl group, C_1-C_6 alkanoyl group or C_2-C_6 alkenyl-carbonyl group; and a group having the formula NR^6R^7.

R^6 and R^7, independently from each other, represent a hydrogen atom, C_1-C_6 alkyl group, C_2-C_6 alkenyl group, C_2-C_6 alkynyl group, C_1-C_6 alkanoyl group or C_2-C_6 alkenyl-carbonyl group, or together with the nitrogen atom to which they are bound form a heterocyclyl group.

Substituent group β represents

an oxo group, hydroxy group, cyclopropyl group, C_1-C_6 alkoxy group, C_1-C_6 alkylthio group, nitro group, halogen atom, cyano group, carboxy group, C_1-C_{10} alkoxy-carbonyl group, C_1-C_6 alkanoyl group, C_2-C_4 alkenyl-carbonyl group, C_2-C_6 alkanoyloxy group, C_2-C_4 alkenyl-carbonyloxy group;

carbamoyl group which may be substituted with a group selected from a C_1-C_4 alkyl group, phenyl group, C_1-C_7 acyl group and C_1-C_4 alkoxy-phenyl group;

thiocarbamoyl group which may be substituted with a C_1-C_4 alkyl group or phenyl group;

carbamoyloxy group which may be substituted with a C_1-C_4 alkyl group or phenyl group;

C_1-C_6 alkanoylamino group, C_1-C_{10} alkoxy-carboxamide group, C_1-C_{10} alkoxy-carbonyloxy group, and

ureido group which may be substituted with a C_1-C_4 alkyl group or phenyl group.

Substituent group γ represents

a heterocyclic group, C_3-C_{10} cycloalkyloxy group, C_6-C_{10} aryloxy group, C_7-C_{19} aralkyloxy group, heterocyclyloxy group, C_3-C_{10} cycloalkylthio group, C_6-C_{10} arylthio group, C_7-C_{19} aralkylthio group, heterocyclylthio group, heterocyclylsulfinyl group, heterocyclylsulfonyl group, C_3-C_6 cycloalkyloxy-carbonyl group, C_6-C_{10} aryloxy-carbonyl group, C_7-C_{19} aralkyloxy-carbonyl group, heterocyclyloxycarbonyl group, C_6-C_{10} aryl-carbonyl group, C_9-C_{10} aryl-carbonyloxy group, C_6-C_{10} aryl-carbonylamino group, C_6-C_{10} aryloxy-carboxamide group, C_7-C_{19} aralkyloxy-carboxamide group, C_6-C_{10} aryloxy-carbonyloxy group, C_7-C_{19} aralkyloxy-carbonyloxy group, C_3-C_{10} cycloalkyloxy-carbonyloxy group and C_6-C_{10} aryl group which may be substituted with a group selected from Substituent group β.

Substituent group δ represents

a hydroxy group, nitro group, cyano group, halogen atom, C_1-C_6 alkyl group, halogeno C_1-C_6 alkyl group, C_1-C_6 alkoxy group, halogeno C_1-C_6 alkoxy group, carboxy group, C_1-C_6 alkanoyl group, C_1-C_6 alkoxy-carbonyl group, C_1-C_6 alkanoylamino group, C_1-C_6 alkylthio group, carbamoyl group, C_1-C_6alkyl-carbamoyl group, C_1-C_6 alkoxy-carbonyl C_1-C_6 alkyl-carbamoyl group, 1,3-diacylguanidino C_1-C_6 alkyl group, a group having the formula NR^6R^7 (R^6 and R^7 are the same as R^6 and R^7 of Substituent group α), C_3-C_6 cycloalkyl group, C_6-C_{10} aryl group and 5-membered heteroaryl group.

Substituent group ϵ represents

a hydroxy group, nitro group, cyano group, halogen atom, C_1-C_{14} alkyl group, cyclopropyl C_1-C_{14} alkyl group, halogeno C_1-C_{14} alkyl group, C_1-C_{14} alkoxy group, halogeno C_1-C_{14} alkoxy group, carboxy group, C_1-C_{14} alkanoyl group, C_1-C_{14} alkoxy-carbonyl group, C_1-C_{14} alkanoylamino group, C_1-C_{14} alkylthio group, carbamoyl group, C_1-C_{14} alkyl-carbamoyl group, C_1-C_{14} alkoxy-carbonyl C_1-C_{14} alkyl-carbamoyl group, 1,3-diacylguanidino C_1-C_{14} alkyl group, a group having the formula NR^6R^7 (R^6 and R^7 are the same as R^6 and R^7 of Substituent group α), C_3-C_6 cycloalkyl group, C_6-C_{10} aryl group and 5-membered heteroaryl group}

or a pharmacologically acceptable salt thereof,

(2) The compound or pharmacologically acceptable salt thereof according to the aforementioned (1), wherein l is 0 and m is an integer of 1 to 3,

(3) The compound or pharmacologically acceptable salt thereof according to the aforementioned (1), wherein l is 0 and m is 2,

(4) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (3), wherein

X and Y together with the carbon atom of ring B form ring A, and ring A is

a 3- to 7-membered heterocyclyl ring

[in the heterocyclyl ring, X and Y, independently from each other, represent any one selected from a carbon atom, a group having the formula NR (R represents a hydrogen atom or a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_1-C_6 alkanoyl group which may be substituted with a group selected from Substituent group α), an oxygen atom, a sulfur atom, a group having the formula SO and a group having the formula SO_2,

the heterocyclyl ring may form a fused ring or spiro ring with a 5- or 6-membered heterocyclyl ring (the heterocyclyl ring includes 1 or 2 oxygen and/or nitrogen atoms as hetero atoms) or 5- or 6-membered cycloalkyl ring, and

ring A, including the fused ring or spiro ring, may be substituted with the same or different 1 to 4 groups selected from the group consisting of an oxo group, a thioxo group, Substituent group α, a cyclopropyl C_1-C_6 alkyl group and a C_1-C_6 alkyl group which may be substituted with 1 to 5 groups selected from Substituent group α]

or

a 3- to 7-membered saturated cycloalkyl ring

(the 3- to 7-membered saturated cycloalkyl ring may be substituted with 1 or 2 groups selected from the group consisting of a hydroxy group, hydroxymethyl group, 1,2-dihydroxyethyl group, 1,2,3-trihydroxypropyl group, 1,2,3,4-tetrahydroxybutyl group and acetylamino group),

(5) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (3), wherein

X and Y represent a group in which X and Y together with the carbon atom of ring B form ring A, and ring A is

a 3- to 7-membered heterocyclyl ring

[in the heterocyclyl ring, X and Y, independently from each other, represent any one selected from a carbon atom, an oxygen atom, a sulfur atom, a group having the formula SO and a group having the formula SO_2,

the heterocyclyl ring may form a fused ring or spiro ring with a 5- or 6-membered heterocyclyl ring (the heterocyclyl ring includes 1 or 2 oxygen and/or nitrogen atoms as hetero atoms) or 5- or 6-membered cycloalkyl ring, and

ring A, including the fused ring or spiro ring, may be substituted with the same or different 1 to 4 groups selected from the group consisting of an oxo group, a thioxo group, Substituent group α and a C_1-C_6 alkyl group which may be substituted with 1 to 4 groups selected from Substituent group α]

or

a 3- to 5-membered saturated cycloalkyl ring

(the 3- to 5-membered saturated cycloalkyl ring may be substituted with 1 or 2 groups selected from the group consisting of a hydroxymethyl group, 1,2-dihydroxyethyl group, 1,2,3-trihydroxypropyl group, 1,2,3,4-tetrahydroxybutyl group and acetylamino group),

(6) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (3), wherein

X and Y represent a group in which X and Y together with the carbon atom of ring B form ring A, and ring A is

a 3- to 7-membered heterocyclyl ring

[the 3- to 7-membered heterocyclyl ring is

oxirane, oxolane, tetrahydrofuran, tetrahydropyran, 1,3-dioxolane, 1,3-dioxane, 1,3-dioxepane, 1,3-dithiolane, 1,3-

dithiane, 1,1,3,3-tetraoxo-1,3-dithiolane, 1,3-oxathiolane, 1,3-oxathiane or 1,3-oxathiepane,

these heterocyclyl rings may form a fused ring or spiro ring with a 5- or 6-membered heterocyclyl ring (the 5- or 6-membered heterocyclyl ring is tetrahydrofuran, tetrahydropyran, pyrrolidine, piperidine or 1,3-dioxane) or cyclohexyl ring, and

ring A, including the fused ring or spiro ring, may be substituted with 1 or 2 groups selected from the group consisting of an oxo group, a thioxo group, Substituent group α (Substituent group α represents a hydroxy group and a group having the formula NR^6R^7, and R^6 and R^7, independently from each other, represent a hydrogen atom or C_1-C_6 alkanoyl group), a methyl group, an ethyl group and a C_1-C_6 alkyl group which is substituted with 1 to 4 hydroxy groups],

or

a cyclopropyl or cyclopentyl ring

(the cyclopropyl or cyclopentyl ring may be substituted with 1 or 2 groups selected from the group consisting of a hydroxymethyl group, 1,2-dihydroxyethyl group, 1,2,3-trihydroxypropyl group, and 1,2,3,4-tetrahydroxybutyl group),

(7) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (3), wherein

X and Y represent a group in which X and Y together with the carbon atom of ring B form ring A, and ring A is

a 3- to 6-membered heterocyclyl ring

{the heterocyclyl ring is

oxirane, tetrahydrofuran,

1,3-dioxolane, 1,3-dioxane,

1,3-dithiolane, 1,3-dithiane,

1,3-oxathiolane, or 1,3-oxathiane,

these heterocyclyl rings may form a fused ring or spiro ring with a 5- or 6-membered heterocyclyl ring (the 5- or 6-membered heterocyclyl ring is tetrahydrofuran, tetrahydropyran or 1,3-dioxane) or cyclohexyl ring, and

ring A, including the fused ring and spiro ring, may be substituted with 1 or 2 groups selected from the group consisting of Substituent group α [Substituent group α represents a hydroxy group and a group having the formula NR^6R^7 (R^6 and R^7, independently from each other, represent a hydrogen atom or acetyl group)], a methyl group, an ethyl group, a hydroxymethyl group, a 1,2-dihydroxyethyl group, a 1,2,3-trihydroxypropyl group and a 1,2,3,4-tetrahydroxybutyl group},

(8) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (7), wherein

n is 0 or 1, and

R^1 is a hydroxy group, halogen atom, C_1-C_6 alkyl group or C_1-C_6 alkoxy group,

(9) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (7), wherein

n is 0 or 1, and

R^1 is a fluorine atom or methyl group,

(10) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (7), wherein n is 0,

(11) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (10), wherein R^2 is a C_1-C_6 alkyl group,

(12) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (10), wherein R^2 is a C_1-C_4 alkyl group,

(13) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (10), wherein R^2 is an ethyl group,

(14) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (13), wherein

R^3 is

a phenyl group which may be substituted with a group selected from Substituent group ε, or

a pyrrolyl group which may be substituted with a group selected from Substituent group ε, and

Substituent group ε is a halogen atom, C_1-C_{14} alkyl group and halogeno C_1-C_{14} alkyl group,

(15) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (13), wherein

R^3 is

a phenyl group which may be substituted with a group selected from Substituent group ε, or

a pyrrolyl group which may be substituted with a group selected from Substituent group ε, and

Substituent group ε is a fluorine atom, chlorine atom, bromine atom, C_3-C_8 alkyl group and halogeno C_4-C_8 alkyl group,

(16) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (13), wherein

R^3 is

a phenyl group which may be substituted with a group selected from Substituent group ε, and

Substituent group ε is a fluorine atom, chlorine atom and C_3-C_8 alkyl group,

(17) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (16), wherein R^5 is a hydrogen atom or C_1-C_6 alkyl group,

(18) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (16), wherein R^5 is a hydrogen atom or methyl group,

(19) The compound or pharmacologically acceptable salt thereof according to any one of the aforementioned (1) to (16), wherein R^5 is a hydrogen atom,

(20) The compounds of the following group selected from the aforementioned (1) or pharmacologically acceptable salt thereof:

ethyl 8-[N-(2-chlorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chlorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2,4-difluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2,4-difluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-hydroxymethyl-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-(1,2,3-trihydroxypropyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-(1,2,3,4-tetrahydroxybutyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(acetylaminomethyl)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3-hydroxy-1,5-dioxaspiro[5.5]undec-7-ene-8-carboxylate,

ethyl 3-acetylamino-9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,5-dioxaspiro[5.5]undec-7-ene-8-carboxylate,

ethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-bis(hydroxymethyl)-1,5-dioxaspiro[5.5]undec-7-ene-8-carboxylate,

ethyl 8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-hexylphenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-heptylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-heptylphenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-bromophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-bromophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-6-methylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-6-methylphenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(hydroxymethyl)-8-[N-(2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(4-fluoro-2-propylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-propylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate, and

ethyl 8-[N-(2-chloro-4-fluorophenyl)-N-methylsulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

(21) A medicament containing the compound or pharmacologically acceptable salt thereof selected from any one of the aforementioned (1) to (20) as an active ingredient,

(22) The medicament according to the aforementioned (21) for use in suppressing intracellular signal transduction or cell activation induced by endotoxin,

(23) The medicament according to the aforementioned (21) for use in suppressing the generation of inflammatory mediators due to intracellular signal transduction or cell activation induced by endotoxin,

(24) The medicament according to the aforementioned (21) for use as a prophylactic or therapeutic agent for a disease due to intracellular signal transduction or cell activation inducted by endotoxin,

(25) The medicament according to the aforementioned (21) for use as a prophylactic and/or therapeutic agent for a disease mediated by an inflammatory mediator, of which generation is induced by endotoxin,

(26) The medicament according to the aforementioned (21) for use as a prophylactic and/or therapeutic agent for a disease mediated by an inflammatory mediator, which is generated due to intracellular signal transduction or cell activation induced by endotoxin,

(27) The medicament according to the aforementioned (21) for use as a prophylactic and/or therapeutic agent for sepsis, and

(i) a method of suppressing intracellular signal transduction induced by endotoxin and suppressing excess generation of inflammatory mediators such as TNF-α which is induced by the intracellular signal transduction, and (ii) a method of preventing and/or treating a disease mediated by intracellular signal transduction and by an inflammatory mediator which is generated due to the intracellular signal transduction, comprising administering an effective amount of the compound according to any one of the aforementioned (1) to (20) or pharmacologically acceptable salt thereof to a warm-blood animal (preferably a human).

EFFECTS OF THE INVENTION

The substituted cycloalkene derivative according to the present invention having the general formula (I) has excellent activity to suppress intracellular signal transduction or cell activation induced by endotoxin and to suppress excess generation of inflammatory mediators such as TNF-α due to the intracellular signal transduction and cell activation, and is useful as a medicament, especially as a prophylactic and/or therapeutic agent for ischemic brain disorder, arteriosclerosis, poor prognosis after coronary angioplasty, heart failure,

diabetes, diabetic complication, joint inflammation, osteoporosis, osteopenia, sepsis, autoimmune disease, tissue disorder and rejection after organ transplantation, bacterial infection, virus infection, gastritis, pancreatitis, nephritis, pneumonia, hepatitis, leukemia and the like, which are induced by the intervention of the intracellular signal transduction or cell activation, and by inflammatory mediators due to the intracellular signal transduction and cell activation.

BEST MODE FOR CARRYING OUT THE INVENTION

"Halogen atom" in the definitions of R^1, Substituent group α, Substituent group β, Substituent group δ and Substituent group ϵ includes, for example, a fluorine atom, chlorine atom, bromine atom or iodine atom.

With respect to R^1, it is preferably a fluorine atom or chlorine atom, more preferably a fluorine atom.

With respect to Substituent group ϵ, it is preferably a fluorine atom, chlorine atom or bromine atom, more preferably a fluorine atom or chlorine atom.

"Alkyl group" in the definitions of the NR group which may be included in ring A, substituent of ring A, R^1, R^2, R^5, R^6, R^7, Substituent group β, Substituent group δ and Substituent group ϵ includes a linear or branched alkyl group.

"C_1-C_6 alkyl group" of "C_1-C_6 alkyl group which may be substituted with a group selected from Substituent group α" in the definition of the NR group which may be included in ring A; "C_1-C_6 alkyl group" of "cyclopropyl C_1-C_6 alkyl group" in the definition of a substituent of ring A; "C_1-C_6 alkyl group" of "C_1-C_6 alkyl group which may be substituted with 1 to 5 groups selected from Substituent group α" in the definition of a substituent of ring A; "C_1-C_6 alkyl group" of "C_1-C_6 alkyl group which may be substituted with a group selected from Substituent group β" in the definitions of R^2 and R^5; and "C_1-C_6 alkyl group" in the definitions of Substituent group δ, R^6 and R^7 are, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, isopentyl, 2-methylbutyl, neopentyl, 1-ethylpropyl, n-hexyl, isohexyl, 4-methylpentyl, 3-methylpentyl, 2-methylpentyl, 1-methylpentyl, 3,3-dimethylbutyl, 2,2-dimethylbutyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 2,3-dimethylbutyl, 2-ethylbutyl group or the like.

Among the "C_1-C_6 alkyl groups", the one with respect to the NR group which may be included in ring A is preferably methyl.

With respect to a substituent of ring A, it is preferably a C_1-C_4 alkyl group.

With respect to R^2, it is preferably a C_1-C_4 alkyl group, more preferably ethyl.

With respect to R^5, it is preferably methyl.

With respect to R^6 and R^7, it is preferably methyl.

With respect to Substituent group δ, it is preferably a C_1-C_4 alkyl group.

C_1-C_{14} alkyl groups of "C_1-C_{14} alkyl group" and "cyclopropyl C_1-C_{14} alkyl group" in the definition of Substituent group ϵ are, for example, the aforementioned "C_1-C_6 alkyl group", octyl, nonyl, decyl, dodecyl, tetradecyl or the like.

With respect to "C_1-C_{14} alkyl group" in the definition of Substituent group ϵ, it is preferably C_3-C_8 alkyl group.

"C_1-C_{20} alkyl group" in the definition of R^1 is, for example, the aforementioned "C_1-C_{14} alkyl group", pentadecyl, hexadecyl, heptadecyl, octadecyl, nonadecyl, icosyl or the like. Preferably, it is a C_1-C_6 alkyl group, and more preferably a methyl group.

"Alkenyl group" in the definitions of the NR group which may be included in ring A, substituent of ring A, R^1, R^2, R^5, R^6, R^7 and Substituent group α is a linear or branched alkenyl group.

"C_3-C_6 alkenyl group" in the definition of R^1 is, for example, 2-propenyl, 1-methyl-2-propenyl, 2-methyl-2-propenyl, 2-ethyl-2-propenyl, 2-butenyl, 1-methyl-2-butenyl, 2-methyl-2-butenyl, 1-ethyl-2-butenyl, 3-butenyl, 1-methyl-3-butenyl, 2-methyl-3-butenyl, 1-ethyl-3-butenyl, 2-pentenyl, 1-methyl-2-pentenyl, 2-methyl-2-pentenyl, 3-pentenyl, 1-methyl-3-pentenyl, 2-methyl-3-pentenyl, 4-pentenyl, 1-methyl-4-pentenyl, 2-methyl-4-pentenyl, 2-hexenyl, 3-hexenyl, 4-hexenyl or 5-hexenyl, preferably a C_3-C_4 alkenyl group.

"C_2-C_6 alkenyl group" of "C_2-C_6 alkenyl group which may be substituted with a group selected from Substituent group α" in the definition of the NR group which may be included in ring A; "C_2-C_6 alkenyl group" of "C_2-C_6 alkenyl group which may be substituted with 1 to 5 groups selected from Substituent group α" in the definition of substituent of ring A; "C_2-C_6 alkenyl group" of "C_2-C_6 alkenyl group which may be substituted with a group selected from Substituent group β" in the definitions of R^2 and R^5; and "C_2-C_6 alkenyl group" in the definitions of R^6 and R^7 are, for example, vinyl or the aforementioned "C_3-C_6 alkenyl group", preferably a C_3-C_4 alkenyl group.

"Alkynyl group" in the definitions of the NR group which may be included in ring A, substituent of ring A, R^1, R^2, R^5, R^6, R^7 and Substituent group α is a linear or branched alkynyl group.

"C_3-C_6 alkynyl group" in the definition of R^1 is, for example, 2-propynyl, 1-methyl-2-propynyl, 2-butynyl, 1-methyl-2-butynyl, 1-ethyl-2-butynyl, 3-butynyl, 1-methyl-3-butynyl, 2-methyl-3-butynyl, 1-ethyl-3-butynyl, 2-pentynyl, 1-methyl-2-pentynyl, 3-pentynyl, 1-methyl-3-pentynyl, 2-methyl-3-pentynyl, 4-pentynyl, 1-methyl-4-pentynyl, 2-methyl-4-pentynyl, 2-hexynyl, 3-hexynyl, 4-hexynyl or 5-hexynyl, preferably a C_3-C_4 alkyl group.

"C_2-C_6 alkynyl group" of "C_2-C_6 alkynyl group which may be substituted with a group selected from Substituent group α" in the definition of the NR group which may be included in ring A; "C_2-C_6 alkynyl group" of "C_2-C_6 alkynyl group which may be substituted with 1 to 5 groups selected from Substituent group α" in the definition of substituent of ring A; "C_2-C_6 alkynyl group" of "C_2-C_6 alkynyl group which may be substituted with a group selected from Substituent group β" in the definitions of R^1 and R^5; and "C_2-C_6 alkynyl group" in the definitions of R^6 and R^7 are, for example, ethynyl or the aforementioned "C_3-C_6 alkynyl group", preferably a C_3-C_4 alkynyl group.

"C_3-C_6 cycloalkyl group" in the definitions of Substituent group δ and Substituent group ϵ are, for example, cyclopropyl, cyclopentyl or cyclohexyl.

"3- to 7-membered cycloalkyl ring" in the definition of ring A may include an unsaturated bond, and such ring is, for example, cyclopropane, cyclobutane, cyclopentane, cyclopentene, cyclohexane, cyclohexene, cyclohexadiene, cycloheptane or cycloheptadiene.

The aforementioned "3- to 7-membered cycloalkyl ring" may form a fused ring or spiro ring with a 3- to 7-membered heterocyclyl ring or 3- to 7-membered cycloalkyl ring, and such cycloalkyl ring is, for example, 2-oxa-bicyclo[4,3,0]nonan-8-ylidene, 3-oxa-bicyclo[3,3,0]heptan-7-ylidene, 2,4-dioxa-spiro[6.6]undecan-8-ylidene, bicyclo[4,3,0]nonan-7-ylidene, spiro[6.6]undecan-8-ylidene or the like.

In addition, the aforementioned "3- to 7-membered cycloalkyl ring" may not form a fused ring or spiro ring, and may be substituted with an oxo group or a thioxo group.

With respect to the aforementioned "cycloalkyl ring", a cycloalkyl ring, fused ring which is fused to the cycloalkyl ring, or spiro ring which is spiro bound to the cycloalkyl ring may be substituted with the same or different 1 to 4 (preferably 1 or 2) groups selected from the group consisting of Substituent group α, cyclopropyl C_1-C_6 alkyl group, C_1-C_6 alkyl group which may be substituted with 1 to 5 groups selected from Substituent group α, C_2-C_6 alkenyl group which may be substituted with 1 to 5 groups selected from Substituent group α and C_2-C_6 alkynyl group which may be substituted with 1 to 5 groups selected from Substituent group α.

Preferred examples of the ring are, 3-hydroxycyclopentane, 4-hydroxycyclohexane, 3-hydroxymethylcyclopentane, 3,4-dihydroxymethylcyclopentane, 4-hydroxymethylcyclohexane, 4,4-dihydroxymethylcyclohexane, 3-(1,2-dihydroxyethyl)cyclopentane, 4-(1,2-dihydroxyethyl) cyclohexane, 3,4-bis(1,2-dihydroxyethyl)cyclopentane, 4,4-bis(1,2-dihydroxyethyl)cyclohexane, 3-(1,2,3-trihydroxypropyl)cyclopentane, 4-(1,2,3-trihydroxypropyl) cyclohexane, 3-(1,2,3,4-tetrahydroxybutyl)cyclopentane, 4-(1,2,3,4-tetrahydroxybutyl)cyclohexane, 3-ethoxycarbonylcyclopentane, 4-ethoxycarbonylcyclohexane, 4,4-diethoxycarbonylcyclchexane, 3-carbamoylcyclopentane, 4-carbamoylcyclohexane, 3-acetylaminocyclopentane, 4-acetylaminocyclohexane, 3,4-diacetylaminomethylcyclopentane, 2,3,4,5-tetrahydroxybicyclo[4,3,0]nonane (the binding position with ring B is the 8-position), 3-oxa-bicyclo [3,3,0]octane (the binding position with ring B is the 7-position), 2,4-dihydroxymethyl-3-oxa-bicyclo[3,3,0]octane (the binding position with ring B is the 7-position), and 2,4-dioxaspiro[5.5]undecane (the binding position with ring B is the 9-position).

"Cycloalkyl ring" in the definition of ring A is, among the aforementioned rings, preferably a 3- to 7-membered cycloalkyl ring which may be substituted with 1 or 2 groups selected from a group consisting of a hydroxy group, hydroxymethyl group, 1,2-dihydroxyethyl group, 1,2,3-trihydroxyethyl group, 1,2,3,4-tetrahydroxybutyl group and acetylamino group, more preferably a 3- to 5-membered saturated cycloalkyl ring which may be substituted with 1 or 2 groups selected from the group consisting of a hydroxymethyl group, 1,2-dihydroxyethyl group, 1,2,3-trihydroxypropyl group, 1,2,3,4-tetrahydroxybutyl group and acetylamino group, and particularly preferably a cyclopropyl or cyclopentyl ring which may be substituted with 1 or 2 groups selected from the group consisting of a hydroxymethyl group, 1,2-dihydroxyethyl group, 1,2,3-trihydroxypropyl group and 1,2,3,4-tetrahydroxybutyl group.

"C_3-C_{10} cycloalkyl group" in the definition of R^1 is, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl.

"C_4-C_{12} cycloalkylalkyl group" in the definition of R^1 is, for example, cyclopropylmethyl, cyclopentylmethyl, cyclohexylmethyl or cycloheptylmethyl, preferably a C_4-C_8 cycloalkylalkyl group, more preferably a C_4-C_7 cycloalkylalkyl group.

With respect to "3- to 7-membered heterocyclyl ring" in the definition of ring A, X and Y included in the ring, independently from each other, represent any one selected from a carbon atom, a group having the formula NR (R represents a hydrogen atom or a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 group or C_1-C_6 alkylcarbonyl group which may be substituted with a group selected from Substituent group α), an oxygen atom, a sulfur atom, a group having the formula SO and a group having the formula SO_2, preferably any one selected from a carbon atom, an oxygen atom, a sulfur atom, a group having the formula SO, and a group having the formula SO_2. The 3- to 7-membered heterocyclyl ring may include an unsaturated bond.

Examples of such ring are, a heterocyclyl ring including a nitrogen atom such as aziridine, azetidine, pyrrolidine, pyrroline, piperidine and imidazolidine; a heterocyclyl ring including an oxygen atom such as oxirane, oxetane, tetrahydrofuran, oxolene, tetrahydropyran, dihydropyran, oxepane, 1,3-dioxclane, 1,3-dioxane and 1,3-dioxepane; a heterocyclyl ring including a sulfur atom, a group having the formula SO or a group having the formula SO_2 such as thiirane, thietane, thiolane, thiolene, thiane, thiepane, 1,3-dithiolane, 1,3-dithiane, 1,3-dithiepane, 1,3-dioxo-1,3-dithiolane, 1,3-dioxo-1,3-dithiane, 1,1,3,3-tetraoxo-1,3-dithiolane and 1,1,3,3-tetraoxo-1,3-dithiane; a heterocyclyl ring including an oxygen atom and a sulfur atom such as 1,3-oxathiolane, 1,3-oxathiane and 1,3-oxathiepane; a heterocyclyl ring including a nitrogen atom and an oxygen atom such as 1,3-oxapyrrolidine and 1,3-oxapyrroline; and a heterocyclyl ring including a nitrogen atom and a sulfur atom such as 1,3-thiapyrrolidine and 1,3-thiapyrroline.

Preferably, it is oxirane, tetrahydrofuran, tetrahydropyran, 1,3-dioxolane, 1,3-dioxane, 1,3-dioxepane, 1,3-dithiolane, 1,3-dithiane, 1,1,3,3-tetraoxo-1,3-dithiolane, 1,3-oxathiolane, 1,3-oxathiane or 1,3-oxathiepane.

More preferably, it is oxirane, tetrahydrofuran, 1,3-dioxolane, 1,3-dioxane, 1,3-dithiolane, 1,3-dithiane, 1,3-oxathiolane or 1,3-oxathiane.

Even more preferably, it is oxirane, 1,3-dioxolane, 1,3-dioxane or 1,3-oxathiolane.

The aforementioned "3- to 7-membered heterocyclyl ring" may form a fused ring or spiro ring with a 3- to 7-membered heterocyclyl ring or 3- to 7-membered cycloalkyl ring, preferably may form a fused ring or spiro ring with a 5- or 6-membered heterocyclyl ring (the heterocyclyl ring includes 1 or 2 oxygen and/or nitrogen atoms as hetero atom) or 5- or 6-membered cycloalkyl ring, and more preferably may form a fused ring or spiro ring with tetrahydrofuran, tetrahydropyran, pyrrolidine, piperidine, 1,3-dioxane or cyclohexyl ring.

Examples of such heterocyclyl ring are 2,4-dioxa-bicyclo [3,3,0]octane (the binding position with ring B is the 3-position), 2,4,7-trioxa-bicyclo[3,3,0]octane (the binding position with ring B is the 3-position), 7,9-dioxa-bicyclo[4,3,0] nonane (the binding position with ring B is the 8-position), 7-aza-2,4-dioxa-bicyclo[3,3,0]octane (the binding position with ring B is the 3-position), 2,4,8,10-tetraoxaspiro[5,5]undecane (the binding position with ring B is the 3-position) and the like. The binding position of these rings with ring B is the same as the aforedescribed one.

In addition, the aforementioned "3- to 7-membered heterocyclyl ring" may not form a fused ring or spiro ring, and may be substituted with an oxo group or a thioxo group.

With respect to the aforementioned "heterocyclyl ring", heterocyclyl ring, fused ring which is fused to the heterocyclyl ring or spiro ring which is spiro bound to the heterocyclyl ring may be substituted with the same or different 1 to 4 (preferably 1 or 2) substituents.

The substituent is a group selected from the group consisting of an oxo group, a thioxo group, Substituent group α, a cyclopropyl C_1-C_6 alkyl group, a C_1-C_6 alkyl group which may be substituted with 1 to 5 groups selected from Substituent group α, a C_2-C_6 alkenyl group which may be substituted with 1 to 5 groups selected from Substituent group α and a

C_2-C_6 alkynyl group which may be substituted with 1 to 5 groups selected from Substituent group α.

The substituent is preferably a group selected from the group consisting of an oxo group, a thioxo group, Substituent group α, a cyclopropyl C_1-C_6 alkyl group and a C_1-C_6 alkyl group which may be substituted with 1 to 5 groups selected from Substituent group α.

More preferably, it is a group selected from the group consisting of an oxo group, a thioxo group, Substituent group α and a C_1-C_6 alkyl group which may be substituted with 1 to 4 groups selected from Substituent group α.

Even more preferably, it is 1 or 2 groups selected from the group consisting of an oxo group, a thioxo group, Substituent group α(Substituent group α is a hydroxy group and a group having the formula NR^6R^7, and R^6 and R^7, independently from each other, represent a hydrogen atom or C_1-C_6 alkylcarbonyl group), a methyl group, an ethyl group and a C_1-C_6 alkyl group substituted with 1 to 4 hydroxy groups.

Further preferably, it is 1 or 2 groups selected from the group consisting of Substituent group α [Substituent group α represents a hydroxy group and a group having the formula NR^6R^7 (R^6 and R^7, independently from each other, represent a hydrogen atom or methylcarbonyl group)], a methyl group, an ethyl group, a hydroxymethyl group, a 1,2-dihydroxyethyl group, a 1,2,3-trihydroxypropyl group and a 1,2,3,4-tetrahydroxybutyl group.

As for such examples,

oxirane, oxolane, tetrahydrofuran (traditional name, oxolane according IUPAC nomenclature), tetrahydropyran (traditional name, oxane according IUPAC nomenclature), 1,3-dioxclane, 1,3-dioxane, 1,3-dioxepane, 1,3-dithiolane, 1,3-dithiane, 1,3-oxathiolane, 1,3-oxathiane, 1,3-oxathiepane, tetrahydrooxazole, tetrahydro-1,3-oxadine, tetrahydrothiazole, tetrahydro-1,3-thiazine, 1,1,3,3-tetraoxo-1,3-dithiane, 2,4,7-trioxa-bicyclo[3,3,0]octane, 2,4-dithia-7-oxa-bicyclo[3,3,0]octane, 2-thia-4,7-dioxa-bicyclo[3,3,0]octane, 2,4,8,10-tetraoxaspiro[5.5]undecane, 2,4-dithia-8,10-dioxaspiro[5.5]undecane, 2-thia-4,8,10-trioxaspiro[5.5]undecane, 2-hydroxytetrahydrofuran, 4-hydroxy-1,3-dioxolane, 4,5-dihydroxy-1,3-dioxolane, 5-hydroxy-1,3-dioxane, 5,5-dihydroxy-1,3-dioxane, 4-hydroxy-1,3-dithiolane, 4,5-dihydroxy-1,3-dithiolane, 5-hydroxy-1,3-dithiane, 5,5-dihydroxy-1,3-dithiane, 4-hydroxy-1,1,3,3-tetraoxo-1,3-dithiolane, 4,5-dihydroxy-1,1,3,3-tetraoxo-1,3-dithiolane, 4-hydroxy-1,3-oxathiolane, 5-hydroxy-1,3-oxathiane, 5,5-dihydroxy-1,3-oxathiane, 6,8-dihydroxy-2,4-dioxa-bicyclo[3,3,0]octane, 6,8-dihydroxy-2,4,7-trioxa-bicyclo[3,3,0]octane, 2,3,4,5-tetrahydroxy-7,9-dioxa-bicyclo[4,3,0]nonane, 6,8-dihydroxy-7-aza-2,4-dioxa-bicyclo[3,3,0]octane, 9-hydroxy-2,4,8,10-tetraoxaspiro[5.5]undecane, 2,3,4,5-tetrahydro-7,9-dithia-bicyclo[4,3,0]nonane, 2,3,4,5-tetrahydro-7-thia-9-oxa-bicyclo[4,3,0]nonane, 2-carboxytetrahydrofuran, 4-carboxy-1,3-dioxolane, 5-carboxy-1,3-dioxane, 4-carboxy-1,3-dithiolane, 5-carboxy-1,3-dithiane, 4-carboxy-1,1,3,3-tetraoxo-1,3-dithiolane, 4-carboxy-1,3-oxathiolane, 5-carboxy-1,3-oxathiane, 2-methoxycarbonyltetrahydrofuran, 4-methoxycarbonyl-1,3-dioxolane, 5-methoxycarbonyl-1,3-dioxane, 5,5-dimethoxycarbonyl-1,3-dioxane, 4-methoxycarbonyl-1,3-dithiolane, 5-methoxycarbonyl-1,3-dithiane, 5,5-dimethoxycarbonyl-1,3-dithiane, 4-methoxycarbonyl-1,1,3,3-tetraoxo-1,3-dithiolane, 4-methoxycarbonyl-1,3-oxathiolane, 5-methoxycarbonyl-1,3-oxathiane, 5,5-dimethoxycarbonyl-1,3-oxathiane, 6,8-dimethoxycarbonyl-2,4-dioxa-bicyclo[3,3,0]octane, 6,8-dimethoxycarbonyl-2,4,7-trioxa-bicyclo[3,3,0]octane, 6,8-dimethoxycarbonyl-7-aza-2,4-dioxa-bicyclo[3,3,0]octane, 8-methoxycarbonyl-2,4,7,9-tetraoxaspiro[5.5]undecane, 2-ethoxycarbonyltetrahydrofuran, 4-ethoxycarbonyl-1,3-dioxolane, 5-ethoxycarbonyl-1,3-dioxane, 5,5-diethoxycarbonyl-1,3-dioxane, 4-ethoxycarbonyl-1,3-dithiolane, 5-ethoxycarbonyl-1,3-dithiane, 5,5-diethoxycarbonyl-1,3-dithiane, 4-ethoxycarbonyl-1,1,3,3-tetraoxo-1,3-dithiolane, 4-ethoxycarbonyl-1,3-oxathiolane, 5-ethoxycarbonyl-1,3-oxathiane, 5,5-diethoxycarbonyl-1,3-oxathiane, 6,8-diethoxycarbonyl-2,4-dioxa-bicyclo[3,3,0]octane, 6,8-diethoxycarbonyl-2,4,7-trioxa-bicyclo[3,3,0]octane, 6,8-diethoxycarbonyl-7-aza-2,4-dioxa-bicyclo[3,3,0]octane, 8-ethoxycarbonyl-2,4,7,9-tetraoxaspiro[5.5]undecane,

2-aminotetrahydrofuran, 4-amino-1,3-dioxolane, 4,5-diamino-1,3-dioxolane, 5-amino-1,3-dioxane, 4-amino-1,3-dithiolane, 4,5-diamino-1,3-dithiolane, 5-amino-1,3-dithiane, 4-amino-1,1,3,3-tetraoxo-1,3-dithiolane, 4-amino-1,3-oxathiolane, 5-amino-1,3-oxathiane,

2-acetylaminotetrahydrofuran, 4-acetylamino-1,3-dioxolane, 4,5-bis(acetylamino)-1,3-dioxolane, 5-acetylamino-1,3-dioxane, 4-acetylamino-1,3-dithiolane, 4,5-bis(acetylamino)-1,3-dithiolane, 5-acetylamino-1,3-dithiane, 4-acetylamino-1,1,3,3-tetraoxo-1,3-dithiolane, 4-acetylamino-1,3-oxathiolane, 5-acetylamino-1,3-oxathiane, 6,8-diacetylamino-2,4-dioxa-bicyclo[3,3,0]octane, 6,8-diacetylamino-2,4,7-trioxa-bicyclo[3,3,0]octane, 6,8-diacetylamino-7-aza-2,4-dioxa-bicyclo[3,3,0]octane, 8-acetylamino-2,4,7,9-tetraoxaspiro[5.5]undecane, 2-methyltetrahydrofuran, 4-methyl-1,3-dioxclane, 4,5-dimethyl-1,3-dioxolane, 5-methyl-1,3-dioxane, 4-methyl-1,3-dithiolane, 4,5-dimethyl-1,3-dithiolane, 5-methyl-1,3-dithiane, 4-methyl-1,1,3,3-tetraoxo-1,3-dithiolane, 4-methyl-1,3-oxathiolane, 5-methyl-1,3-oxathiane,

5,5-dimethyl-1,3-dioxane, 5,5-dimethyl-1,3-dithiane, 5,5-dimethyl-1,3-oxathiane,

2-ethyltetrahydrofuran, 4-ethyl-1,3-dioxolane, 4,5-diethyl-1,3-dioxolane, 5-ethyl-1,3-dioxane, 4-ethyl-1,3-dithiolane, 4,5-diethyl-1,3-dithiolane, 5-ethyl-1,3-dithiane, 4-ethyl-1,1,3,3-tetraoxo-1,3-dithiolane, 4-ethyl-1,3-oxathiolane, S-ethyl-1,3-oxathiane,

2-hydroxymethyltetrahydrofuran, 4-hydroxymethyl-1,3-dioxolane, 5-hydroxymethyl-1,3-dioxane, 5,5-dihydroxymethyl-1,3-dioxane, 4-hydroxymethyl-1,3-dithiolane, 5-hydroxymethyl-1,3-dithiane, 5,5-dihydroxymethyl-1,3-dithiane, 4-hydroxymethyl-1,1,3,3-tetraoxo-1,3-dithiolane, 4-hydroxymethyl-1,3-oxathiolane, 5-hydroxymethyl-1,3-oxathiane, 5,5-dihydroxymethyl-1,3-oxathiane, 4,5-dihydroxymethyl-1,3-dioxolane, 4,5-dihydroxymethyl-1,3-dithiolane, 4,5-dihydroxymethyl-1,3-oxathiolane, 5,5-dihydroxymethyl-1,3-dioxane, 5,5-dihydroxymethyl-1,3-dithiane, 5,5-dihydroxymethyl-1,3-oxathiane, 6,8-dihydroxymethyl-2,4,7-trioxa-bicyclo[3,3,0]octane, 6,8-dihydroxymethyl-2,4-dithia-7-oxa-bicyclo[3,3,0]octane, 6,8-dihydroxymethyl-2-thia-4,7-dioxa-bicyclo[3,3,0]octane, 6-oxo-8-hydroxymethyl-2,4,7-trioxa-bicyclo[3,3,0]octane,

2-(1,2-dihydroxyethyl)tetrahydrofuran, 4-(1,2-dihydroxyethyl)-1,3-dioxolane, 5-(1,2-dihydroxyethyl)-1,3-dioxane, 5,5-bis(1,2-dihydroxyethyl)-1,3-dioxane, 4-(1,2-dihydroxyethyl)-1,3-dithiolane, 5-(1,2-dihydroxyethyl)-1,3-dithiane, 5,5-bis(1,2-dihydroxyethyl)-1,3-dithiane, 4-(1,2-dihydroxyethyl)-1,1,3,3-tetraoxo-1,3-dithiolane, 4-(1,2-dihydroxyethyl)-1,3-oxathiolane, 5-(1,2-dihydroxyethyl)-1,3-oxathiane, 5,5-bis(1,2-dihydroxyethyl)-1,3-oxathiane,

4,5-bis(1,2-dihydroxyethyl)-1,3-dioxolane, 4,5-bis(1,2-dihydroxyethyl)-1,3-dithiolane, 4,5-bis(1,2-dihydroxyethyl)-1,3-oxathiolane,

4,5-bis(1-hydroxyethyl)-1,3-dioxolane, 4,5-bis(1-hydroxypropyl)-1,3-dioxolane,

2-(1,2,3-trihydroxypropyl)tetrahydrofuran, 4-(1,2,3-trihydroxypropyl)-1,3-dioxolane, 5-(1,2,3-trihydroxypropyl)-1,3-dioxane, 5,5-bis(1,2,3-trihydroxypropyl)-1,3-dioxane, 4-(1,2,3-trihydroxypropyl)-1,3-dithiolane, 5-(1,2,3-trihydroxypropyl)-1,3-dithiane, 5,5-bis(1,2,3-trihydroxypropyl)-1,3-dithiane, 4-(1,2,3-trihydroxypropyl)-1,1,3,3-tetraoxo-1,3-dithiolane, 4-(1,2,3-trihydroxypropyl)-1,3-oxathiolane, 5-(1,2-dihydroxyethyl)-1,3-oxathiane, 5,5-bis(1,2,3-trihydroxypropyl)-1,3-oxathiane,

2-(1,2,3,4-tetrahydroxybutyl)tetrahydrofuran, 4-(1,2,3,4-tetrahydroxybutyl)-1,3-dioxolane, 5-(1,2,3,4-tetrahydroxybutyl)-1,3-dioxane, 5,5-bis(1,2,3,4-tetrahydroxybutyl)-1,3-dioxane, 4-(1,2,3,4-tetrahydroxybutyl)-1,3-dithiolane, 5-(1,2,3,4-tetrahydroxybutyl)-1,3-dithiane, 5,5-bis(1,2,3,4-tetrahydroxybutyl)-1,3-dithiane, 4-(1,2,3,4-tetrahydroxybutyl)-1,1,3,3-tetraoxo-1,3-dithiolane, 4-(1,2,3,4-tetrahydroxybutyl)-1,3-oxathiolane, 5-(1,2,3,4-tetrahydroxybutyl)-1,3-oxathiane, 5,5-bis(1,2,3,4-tetrahydroxybutyl)-1,3-oxathiane,

2-acetylaminomethyltetrahydrofuran, 4-acetylaminomethyl-1,3-dioxolane, 4,5-diacetylaminomethyl-1,3-dioxolane, 5-acetylaminomethyl-1,3-dioxane, 4-acetylaminomethyl-1,3-dithiolane, 4,5-diacetylaminomethyl-1,3-dithiolane, 5-acetylaminomethyl-1,3-dithiane, 4-acetylaminomethyl-1,1,3,3-tetraoxo-1,3-dithiolane, 4-acetylaminomethyl-1,3-oxathiolane, 5-acetylaminomethyl-1,3-oxathiane,

4,5-diacetylaminomethyl-1,3-dioxolane, 4,5-diacetylaminomethyl-1,3-dithiolane, 4,5-diacetylaminomethyl-1,3-oxathiolane, 2-vinyltetrahydrofuran, 4-vinyl-1,3-dioxolane, 4,5-divinyl-1,3-dioxolane, 5-vinyl-1,3-dioxane, 4-vinyl-1,3-dithiolane, 4,5-divinyl-1,3-dithiolane, 5-vinyl-1,3-dithiane, 4-vinyl-1,1,3,3-tetraoxo-1,3-dithiolane, 4-vinyl-1,3-oxathiolane, 5-vinyl-1,3-oxathiane,

2-propenyltetrahydrofuran, 4-propenyl-1,3-dioxolane, 4,5-dipropenyl-1,3-dioxolane, 5-propenyl-1,3-dioxane, 4-propenyl-1,3-dithiolane, 4,5-dipropenyl-1,3-dithiolane, 5-propenyl-1,3-dithiane, 4-propenyl-1,1,3,3-tetraoxo-1,3-dithiolane, 4-propenyl-1,3-oxathiolane, 5-propenyl-1,3-oxathiane, 2-propynyltetrahydrofuran, 4-propynyl-1,3-dioxolane, 4,5-dipropynyl-1,3-dioxolane, 5-propynyl-1,3-dioxane, 4-propynyl-1,3-dithiolane, 4,5-dipropynyl-1,3-dithiclane, 5-propynyl-1,3-dithiane, 4-propynyl-1,1,3,3-tetraoxo-1,3-dithiolane, 4-propynyl-1,3-oxathiolane and 5-propynyl-1,3-oxathiane can be mentioned.

"C_6-C_{10} aryl group" of "C_6-C_{10} aryl group which may be substituted with a group selected from Substituent group β" in the definition of Substituent group γ; and "C_6-C_{10} aryl group" in the definitions of Substituent group δ and Substituent group ϵ are, for example, phenyl or naphthyl.

With respect to the "C_6-C_{10} aryl group which may be substituted with a group selected from Substituent group β", the "C_6-C_{10} aryl group" is substituted with a substituent selected from Substituent group β at a substitutable position, the substituent is not limited to one, and may be the same or different plural (2 to 4) substituents.

"5- or 6-membered heteroaryl group" in the definition of R^3 includes 1 to 3 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom. As for such heteroaryl, for example, furyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridyl, piridazinyl, pyrimidinyl and pyradinyl can be mentioned, and it is preferably furyl, thienyl, pyrrolyl, pyridyl or pyrimidinyl, more preferably pyrrolyl.

"5-membered heteroaryl group" in the definitions of Substituent group δ and Substituent group ϵ is, for example, 1,2,3-triazolyl, 1,2,4-triazolyl, tetrazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, thiadiazolyl, thienyl or furyl.

"Halogeno C_1-C_6 alkyl group" in the definition of Substituent group δ is, for example, trifluoromethyl or trifluoroethyl.

"Halogeno C_1-C_{14} alkyl group" in the definition of Substituent group ϵ is, for example, the aforementioned "halogeno C_1-C_6 alkyl group", 4,4,4-trifluorobutyl, 5,5,5-trifluoropentyl, 6,6,6-trifluorohexyl, 7,7,7-trifluoroheptyl or 8,8,8-trifluorooctyl, preferably a halogeno C_4-C_8 alkyl group.

"C_1-C_6 alkoxy group" in the definitions of Substituent group α, Substituent group β and Substituent group δ represents a group in which an oxygen atom is bound to the aforementioned "C_1-C_6 alkyl group", for example, methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, s-butoxy, t-butoxy, pentoxy, isopentoxy, 2-methylbutoxy, 1-ethylpropoxy, 2-ethylpropoxy, neopentoxy, hexyloxy, 4-methylpentoxy, 3-methylpentoxy, 2-methylpentoxy, 3,3-dimethylbutoxy, 2,2-dimethylbutoxy, 1,1-dimethylbutoxy, 1,2-dimethylbutoxy, 1,3-dimethylbutoxy or 2,3-dimethylbutoxy, preferably a C_1-C_4 alkoxy group, and more preferably C_1-C_2 alkoxy group.

"C_1-C_{14} alkoxy group" in the definition of Substituent group ϵ represents a group in which an oxygen atom is bound to the aforementioned "C_1-C_{14} alkyl group", for example, the aforementioned "C_1-C_6 alkoxy group", octyloxy, nonyloxy, decyloxy, dodecyloxy, tetradecyloxy or the like, preferably a C_1-C_{10} alkoxy group, and more preferably a C_4-C_8 alkoxy group.

"Halogeno C_1-C_6 alkoxy group" in the definitions of Substituent group α and Substituent group δ represents a group in which one or two or more hydrogen atoms of the aforementioned "C_1-C_6 alkyl group" are substituted with the aforementioned "halogen atom". Preferably, it is a halogeno C_1-C_4 alkoxy group, more preferably difluoromethoxy, trifluoromethoxy or 2,2,2-trifluoroethoxy, and even more preferably trifluoromethoxy.

"Halogeno C_1-C_{14} alkoxy group" in the definition of Substituent group ϵ represents a group in which one or two or more hydrogen atoms of the aforementioned "C_1-C_{14} alkyl group" are substituted with the aforementioned "halogen atom". Preferably, it is a halogeno C_1-C_{10} alkoxy group, more preferably a halogeno C_4-C_8 alkoxy group, and even more preferably 4,4,4-trifluorobutoxy, 5,5,5-trifluoropentyloxy, 6,6,6-trifluorohexyloxy, 7,7,7-trifluoroheptyloxy or 8,8,8-trifluorooctyloxy.

"C_3-C_{10} cycloalkyloxy group" in the definition of Substituent group γ is, for example, cyclopropyloxy, cyclohexyloxy or the like.

"C_6-C_{10} aryloxy group" in the definition of Substituent group γ is, for example, phenoxy or naphthyloxy.

"C_7-C_{19} aralkyloxy group" in the definition of Substituent group γ is, for example, benzyloxy, 1-phenylethyloxy, 2-phenylethyloxy, benzhydryloxy or 1-naphthylmethyloxy.

"C_1-C_6 alkylthio group" in the definitions of Substituent group β and Substituent group δ represents a group in which a sulfur atom is bound to the aforementioned "C_1-C_6 alkyl group", and the sulfur atom may be oxidized. Preferably, it is a C_1-C_4 alkylthio group, for example, methylthio, ethylthio, n-propylthio, n-butylthio, methylsulfinyl or methylsulfonyl.

With respect to "C_1-C_{14} alkylthio group" in the definition of Substituent group ϵ, the sulfur atom to which the alkyl group is bound may be oxidized, and it is for example, the

aforementioned "C_1-C_6 alkylthio group", n-heptylthio, 3-methylhexylthio, n-octylthio, 2,4-dimethylhexylthio, n-octylthio, or 2,3,6-trimethylheptylthio, preferably a C_1-C_{10} alkylthio group, and more preferably a C_4-C_8 alkylthio group.

With respect to "C_3-C_{10} cycloalkylthio group" in the definition of Substituent group γ, the sulfur atom may be oxidized, and it is for example, cyclopropylthio, cyclohexylthio, cyclopentylsulfinyl or cyclohexylsulfonyl.

With respect to "C_6-C_{10} arylthio group" in the definition of Substituent group γ, the sulfur atom may be oxidized, and it is for example, phenylthio, naphthylthio, phenylsulfinyl or phenylsulfonyl.

With respect to "C_7-C_{19} aralkylthio group" in the definition of Substituent group γ, the sulfur atom may be oxidized, and it is for example, benzylthio, phenylethylthio, benzhydrylthio, benzylsulfinyl or benzylsulfonyl.

"C_1-C_6 alkanoyl group" in the definitions of R^6, R^7, Substituent group β and Substituent group δ represents a group in which a hydrogen atom or C_1-C_5 alkyl group is bound to a carbonyl group, and is for example, formyl, acetyl, propionyl, butyryl, valeryl or pyvaloyl.

"C_1-C_{14} alkanoyl group" in the definition of Substituent group ϵ is, for example, the aforementioned "C_1-C_6 alkanoyl group", octanoyl, decanoyl, dodecanoyl or tetradecanoyl.

"C_2-C_4 alkenyl-carbonyl group" in the definition of Substituent group β is, for example, acryloyl or crotonoyl.

"C_2-C_6 alkenyl-carbonyl group" in the definitions of R^6 and R^7 is, for example, the aforementioned "C_2-C_4 alkenyl-carbonyl group", 1,3-butadienylcarbonyl or 3-methyl-2-butenylcarbonyl.

"C_6-C_{10} aryl-carbonyl group" in the definition of Substituent group γ is, for example, benzoyl, naphthoyl or phenylacetyl.

"C_1-C_6 alkoxy-carbonyl group" in the definitions of Substituent group α and Substituent group δ represents a group in which the aforementioned "C_1-C_6 alkoxy group" is bound to a carbonyl group, and is for example, methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, isopropoxycarbonyl, n-butoxycarbonyl, isobutoxycarbonyl, tert-butoxycarbonyl or the like.

"C_1-C_{10} alkoxy-carbonyl group" in the definition of Substituent group β is, for example, the aforementioned "C_1-C_6 alkoxycarbonyl group", heptyloxy, octyloxy, nonyloxy or decyloxy.

"C_1-C_{14} alkoxy-carbonyl group" in the definition of Substituent group ϵ is, for example, the aforementioned "C_1-C_{10} alkoxy-carbonyl group", dodecyloxycarbonyl or tetradecyloxycarbonyl, preferably a C_1-C_{10} alkoxy-carbonyl group, and more preferably a C_4-C_8 alkoxy-carbonyl group.

"C_3-C_6 cycloalkyloxycarbonyl group" in the definition of Substituent group γ is, for example, cyclopropyloxycarbonyl, cyclopentyloxycarbonyl, cyclohexyloxycarbonyl or norbornyloxycarbonyl.

"C_6-C_{10} aryloxy-carbonyl group" in the definition of Substituent group γ is, for example, phenoxycarbonyl or naphthyloxycarbonyl.

"C_7-C_{19} aralkyloxy-carbonyl group" in the definition of Substituent group γ is, for example, benzyloxycarbonyl, benzhydryloxycarbonyl or 2-phenethyloxycarbonyl.

"C_2-C_6 alkanoyloxy group" in the definition of Substituent group β represents a group in which the C_2-C_6 alkanoyl group is bound to an oxygen atom, and is for example, acetoxy, propionyloxy, butyryloxy, valeryloxy or pivaloyloxy.

"C_1-C_{10} alkoxy-carbonyloxy group" in the definition of Substituent group β is, for example, methoxycarbonyloxy, ethoxycarbonyloxy, n-propoxycarbonyloxy, isopropoxycarbonyloxy, n-butoxycarbonyloxy, tert-butoxycarbonyloxy, n-pentyloxycarbonyloxy or n-hexyloxycarbonyloxy.

"C_6-C_{10} aryl-carbonyloxy group" in the definition of Substituent group γ is, for example, benzoyloxy, naphthyloxy or phenylacetoxy.

"Carbamoyl group which may be substituted with a group selected from a C_1-C_6 alkyl group, C_2-C_6 alkenyl group, C_2-C_6 alkynyl group, C_1-C_6 alkanoyl group or C_2-C_6 alkenyl-carbonyl group" in the definition of Substituent group α is a carbamoyl group or cyclic aminocarbonyl group which may be substituted with 1 or 2 substituents selected from C_1-C_6 alkyl groups such as methyl, ethyl, propyl and the like, C_2-C_6 alkenyl groups such as vinyl, allyl, isopropenyl and the like, C_2-C_6 alkynyl groups such as ethynyl and the like, C_1-C_6 alkanoyl groups such as acetyl and the like, and C_2-C_6 alkenyl-carbonyl groups such as acryloyl and the like, preferably, specifically for example, a carbamoyl group or cyclic aminocarbonyl group which may be substituted with 1 or 2 substituents selected from a C_1-C_6 alkyl group and a C_1-C_6 alkanoyl group, more preferably a carbamoyl group or cyclic aminocarbonyl group which is substituted with 1 or 2 C_1-C_2 alkanoyl groups. Specifically, it is carbamoyl, N-methylcarbamoyl, N-ethylcarbamoyl, N,N-dimethylcarbamoyl, N,N-diethylcarbamoyl or N-acetylcarbamoyl, preferably N-acetyl carbamoyl.

"Carbamoyl group which may be substituted with a group selected from a C_1-C_4 alkyl group, phenyl group, C_1-C_7 acyl group and C_1-C_4 alkoxyphenyl group" in the definition of Substituent group β is a carbamoyl group or cyclic aminocarbonyl group which may be substituted with 1 or 2 substituents selected from C_1-C_4 alkyl groups such as methyl, ethyl and the like, phenyl group, C_1-C_7 acyl groups such as acetyl, propionyl, benzoyl and the like, and C_1-C_4 alkoxyphenyl groups such as methoxyphenyl and the like, specifically for example, carbamoyl, N-methylcarbamoyl, N-ethylcarbamoyl, N,N-dimethylcarbamoyl, N,N-diethylcarbamoyl, N-phenylcarbamoyl, N-acetylcarbamoyl, N-benzoylcarbamoyl, N-(p-methoxyphenyl)carbamoyl, 1-pyrrolidinylcarbonyl, piperidinocarbonyl, 1-piperadinylcarbonyl or morpholinocarbonyl.

"Thiocarbamoyl group which may be substituted with a C_1-C_4 alkyl group or phenyl group" in the definition of Substituent group β is a thiocarbamoyl group which may be substituted with 1 or 2 substituents selected from C_1-C_4 alkyl groups such as methyl, ethyl and the like, and a phenyl group, specifically for example, thiocarbamoyl, N-methylthiocarbamoyl or N-phenylthiocarbamoyl.

"Carbamoyloxy group which may be substituted with a C_1-C_4 alkyl group or phenyl group" in the definition of Substituent group β is a carbamoyloxy group which may be substituted with 1 or 2 substituents selected from C_1-C_4 alkyl groups such as methyl, ethyl and the like, and a phenyl group, specifically for example, carbamoyloxy, N-methyl carbamoyloxy, N,N-dimethyl carbamoyloxy, N-ethylcarbamoyloxy or N-phenyl carbamoyloxy.

With respect to "group having the formula NR^6R^7" in the definitions of Substituent group α, Substituent group δ and Substituent group ϵ, R^6 and R^7, independently from each other, represent a hydrogen atom, C_1-C_6 alkyl group, C_2-C_6 alkenyl group, C_2-C_6 alkynyl group, C_1-C_6 alkanoyl group or C_2-C_6 alkenyl-carbonyl group, or, together with the nitrogen atom to which R^6 and R^7 are bound, form a heterocyclyl group. Preferably, it is a group in which R^6 and R^7 are a hydrogen atom, C_1-C_6 alkyl group or C_1-C_6 alkanoyl group, more preferably a group in which R^6 and R^7 are a hydrogen atom, C_1-C_4 alkyl group or C_1-C_4 alkanoyl group, even more preferably a group in which R^6 and R^7 are a hydrogen atom or

C_1-C_2 alkanoyl group. Specifically it is amino, methylamino, ethylamino, dimethylamino, diethylamino or acetylamino, preferably acetylamino.

"C_1-C_6 alkanoylamino group" in the definitions of Substituent group β and Substituent group δ is, for example, acetamide, propionamide, butyramide, valeroamide or pivaloamide.

"C_1-C_{14} alkanoylamino group" in the definition of Substituent group ϵ is, for example, the aforementioned "C_1-C_6 alkanoylamino group", octanoylamino, decanoylamino, dodecanoylamino or tetradecanoylamino.

"C_1-C_{10} alkoxy-carboxamide group" in the definition of Substituent group β is, for example, methoxycarboxamide, ethoxycarboxamide or tert-butoxycarboxamide.

"Ureido group which may be substituted with a C_1-C_4 alkyl group or phenyl group" in the definition of Substituent group β is, for example, an ureido group which may be substituted with 1 to 3 (preferably 1 or 2) substituents selected from C_1-C_4 alkyl groups such as a methyl group, ethyl group and the like, and a phenyl group, and it is for example, ureido, 1-methylureido, 3-methylureido, 3,3-dimethylureido, 1,3-dimethylureido or 3-phenylureido.

"C_6-C_{10} aryl-carbonylamino group" in the definition of Substituent group γ is, for example, benzamide, naphthoamide or phthalimide.

"C_6-C_{10} aryloxy-carboxamide group" in the definition of Substituent group γ is, for example, phenoxycarboxamide.

"C_7-C_{19} aralkyloxy-carboxamide group" in the definition of Substituent group γ is, for example, benzyloxycarboxamide or benzhydryloxycarboxamide.

"C_3-C_{10} cycloalkyloxy-carbonyloxy group" in the definition of Substituent group γ is, for example, cyclopropyloxycarbonyloxy or cyclohexyloxycarbonyloxy.

"C_6-C_{10} aryloxy-carbonyloxy group" in the definition of Substituent group γ is, for example, phenoxycarbonyloxy or naphthyloxycarbonyloxy.

"C_7-C_{19} aralkyloxy-carbonyloxy group" in the definition of Substituent group γ is, for example, benzyloxycarbonyloxy, 1-phenylethyloxycarbonyloxy, 2-phenylethyloxycarbonyloxy or benzhydryloxycarbonyloxy.

"Heterocyclyl group" in the definition of Substituent group γ; and "heterocyclyl group" of "heterocyclyloxy group", "heterocyclylthio group", "heterocyclylsulfinyl group", "heterocyclylsulfonyl group" and "heterocyclyloxycarbonyl group" represent a 5- to 8-membered ring (preferably 5- or 6-membered ring) group or a fused ring group thereof, which contains 1 to several (preferably 1 to 4) hetero atoms such as nitrogen atoms (may be oxidized), oxygen atoms and sulfur atoms. Examples of such "heterocyclyl group" are pyrrolyl, pyrazolyl, imidazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, tetrazolyl, furyl, thienyl, oxazolyl, isoxazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, thiazolyl, isothiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, pyranyl, thiopyranyl, dioxynyl, dioxolyl, quinolyl, pyrido[2,3-d]pyrimidyl, 1,5-, 1,6-, 1,7-, 1,8-, 2,6- or 2,7-naphthylidyl group, thieno[2,3-d]pyridyl, benzopyranyl, tetrahydrofuryl, tetrahydropyranyl, dioxolanyl and dioxanyl.

These heterocyclyl groups may be substituted at substitutable positions with 1 to 3 substituents selected from C_1-C_4 alkyl groups such as methyl, ethyl and the like, a hydroxy group, an oxo group and C_1-C_4 alkoxy groups such as methoxy, ethoxy and the like.

"C_1-C_6 alkyl-carbamoyl group" in the definition of Substituent group δ is, for example, methylcarbamoyl, dimethylcarbamoyl or propylcarbamoyl.

"C_1-C_{14} alkyl-carbamoyl group" in the definition of Substituent group ϵ is, for example, the aforementioned "C_1-C_6 alkyl-carbamoyl group", octylcarbamoyl, decylcarbamoyl, dodecylcarbamoyl or tetradecylcarbamoyl, preferably a C_1-C_{10} alkyl-carbamoyl group, and more preferably a C_4-C_8 alkyl-carbamoyl group.

"C_1-C_6 alkoxy-carbonyl C_1-C_6 alkyl-carbamoyl group" in the definition of Substituent group δ is, for example, butoxycarbonylmethylcarbamoyl or ethoxycarbonylmethylcarbamoyl.

"C_1-C_{14} alkoxy-carbonyl C_1-C_{14} alkyl-carbamoyl group" in the definition of Substituent group ϵ is, for example, the aforementioned "C_1-C_6 alkoxy-carbonyl C_1-C_6 alkyl-carbamoyl group" or octyloxycarbonylmethylcarbamoyl, preferably a C_1-C_{10} alkoxy-carbonyl C_1-C_{10} alkyl-carbamoyl group, and more preferably a C_4-C_8 alkoxy-carbonyl C_4-C_8 alkyl-carbamoyl group.

"1,3-diacylguanidino C_1-C_6 alkyl group" in the definition of Substituent group δ is, for example, 1,3-diacetylguanidinomethyl or 1,3-bis-tert-butoxycarbonylguanidinomethyl.

"1,3-diacylguanidino C_1-C_{14} alkyl group" in the definition of Substituent group ϵ is, for example, the aforementioned "1,3-diacylguanidino C_1-C_6 alkyl group", 1,3-diacetylguanidinooctyl or 1,3-bis-tert-butoxycarbonylguanidinooctyl, preferably a 1,3-diacylguanidino C_1-C_{10} alkyl group, and more preferably a 1,3-diacylguanidino C_4-C_8 alkyl group.

X and Y represent a group in which X and Y together with the carbon atom of ring B to which they are bound form ring A, respectively represent a hydrogen atom, or X and Y together represent a substituent of ring B (the substituent is an oxo group or a thioxo group), and preferably represent a group in which X and Y together with the carbon atom of ring B to which they are bound form ring A, or respectively represent a hydrogen atom.

In a preferred example, in the case where X and Y represent a group in which X and Y together with the carbon atom of ring B to which they are bound form ring A, ring A is a 3- to 7-membered heterocyclyl ring or 3- to 7-membered saturated cycloalkyl ring.

With respect to the heterocyclyl ring, X and Y included in the ring, independently from each other, represent any one selected from a carbon atom, a group having the formula NR (R represents a hydrogen atom, a C_1-C_6 alkyl group which may be substituted with a group selected from Substituent group α, a C_2-C_6 alkenyl group which may be substituted with a group selected from Substituent group α, a C_2-C_6 alkynyl group which may be substituted with a group selected from Substituent group α or a C_1-C_6 alkanoyl group which may be substituted with a group selected from Substituent group α), an oxygen atom, a sulfur atom, a group having the formula SO and a group having the formula SO_2,

may form a fused ring or spiro ring with a 5- or 6-membered heterocyclyl ring (the heterocyclyl ring includes 1 or 2 oxygen and/or nitrogen atoms as hetero atom) or 5- or 6-membered cycloalkyl ring,

either ring of the heterocyclyl ring, or the fused ring which is fused to the heterocyclyl ring or the spiro ring which is spiro bound to the heterocyclyl ring, may be substituted with the same or different 1 to 4 groups selected from the group consisting of an oxo group, a thioxo group, Substituent group α, a cyclopropyl C_1-C_6 alkyl group and a C_1-C_6 alkyl group which may be substituted with 1 to 5 groups selected from Substituent group α.

The 3- to 7-membered saturated cycloalkyl ring may be substituted with 1 or 2 groups selected from the group consisting of a hydroxy group, a hydroxymethyl group, a 1,2-

dihydroxyethyl group, a 1,2,3-trihydroxypropyl group, a 1,2,3,4-tetrahydroxybutyl group and an acetylamino group.

Ring A is, more preferably, a 3- to 7-membered heterocyclyl ring or 3- to 5-membered cycloalkyl ring.

With respect to the heterocyclyl ring which is a more preferred example of ring A, X and Y included in the ring, independently from each other, represent any one selected from a carbon atom, an oxygen atom, a sulfur atom, a group having the formula SO and a group having the formula SO_2, may form a fused ring or spiro ring with a 5- or 6-membered heterocyclyl ring (the heterocyclyl ring includes 1 or 2 oxygen and/or nitrogen atoms as hetero atom) or 5- or 6-membered cycloalkyl ring, and

either ring of the heterocyclyl ring, or the fused ring which is fused to the heterocyclyl ring or the spiro ring which is spiro bound to the heterocyclyl ring, may be substituted with the same or different 1 to 4 groups selected from an oxo group, a thioxo group, Substituent group α and a C_1-C_6 alkyl group which may be substituted with 1 to 4 groups selected from Substituent group α.

The 3- to 5-membered cycloalkyl ring may be substituted with 1 or 2 groups selected from the group consisting of a hydroxymethyl group, a 1,2-dihydroxyethyl group, a 1,2,3-trihydroxypropyl group, a 1,2,3,4-tetrahydroxybutyl group and an acetylamino group.

Ring A is, more preferably, the heterocyclyl ring or the undermentioned cyclopropyl or cyclopentyl ring described below.

Examples of such heterocyclyl ring are,
oxirane, tetrahydrofuran, tetrahydropyrane,
1,3-dioxolane, 1,3-dioxane, 1,3-dioxepane,
1,3-dithiolane, 1,3-dithiane,
1,1,3,3-tetraoxo-1,3-dithiolane,
1,3-oxathiolane, 1,3-oxathiane or 1,3-oxathiepane,

these heterocyclyl rings may form a fused ring or spiro ring with a 5- or 6-membered heterocyclyl ring (the heterocyclyl ring is tetrahydrofuran, tetrahydropyrane, pyrrolidine, piperidine or 1,3-dioxane) or cyclohexyl ring,

either ring of the heterocyclyl ring, or the fused ring which is fused to the heterocyclyl ring or the spiro ring which is spiro bound to the heterocyclyl ring, may be substituted with 1 or 2 groups selected from the group consisting of an oxo group, a thioxo group, Substituent group α (Substituent group α represents a hydroxy group and a group having the formula NR^6R^7, and R^6 and R^7, independently from each other, represent a hydrogen atom or a C_1-C_6 alkanoyl group), a methyl group, an ethyl group and a C_1-C_6 alkyl group which is substituted with 1 to 4 hydroxy groups.

In addition, the cyclopropyl or cyclopentyl ring is a cyclopropyl or cyclopentyl ring which may be substituted with 1 or 2 groups selected from the group consisting of a hydroxymethyl group, a 1,2-dihydroxyethyl group, a 1,2,3-trihydroxypropyl group and a 1,2,3,4-tetrahydroxybutyl group.

Ring A is, further preferably for example,

oxirane, tetrahydrofuran, 1,3-dioxolane, 1,3-dioxane, 1,3-dithiolane, 1,3-dithiane, 1,3-oxathiolane or 1,3-oxathiane, these heterocyclyl rings may form a fused ring or spiro ring with a 5- or 6-membered heterocyclyl ring (the heterocyclyl ring is tetrahydrofuran, tetrahydropyrane or 1,3-dioxane) or cyclohexyl ring, and

either ring of the heterocyclyl ring, or the fused ring which is fused to the heterocyclyl ring or the spiro ring which is spiro bound to the heterocyclyl ring, may be substituted with 1 or 2 groups selected from the group consisting of Substituent group α [Substituent group α represents a hydroxy group and a group having the formula NR^6R^7 (R^6 and R^7, independently from each other, represent a hydrogen atom or acetyl group)], a methyl group, an ethyl group, a hydroxymethyl group, a 1,2-dihydroxyethyl group, a 1,2,3-trihydroxypropyl group and a 1,2,3,4-tetrahydroxybutyl group.

Ring A is, particularly preferably,

oxirane, 1,3-dioxolane, 1,3-dioxane or 1,3-oxathiolane, these heterocyclyl rings may form a fused ring or spiro ring with a 5- or 6-membered heterocyclyl ring (the heterocyclyl ring is tetrahydrofuran, tetrahydropyrane or 1,3-dioxane) or cyclohexyl ring, and

either ring of the heterocyclyl ring, or the fused ring which is fused to the heterocyclyl ring or the spiro ring which is spiro bound to the heterocyclyl ring may be substituted with 1 or 2 groups selected from the group consisting of Substituent group α [Substituent group α represents a hydroxy group and a group having the formula NR^6R^7 (R^6 and R^7, independently from each other, represent a hydrogen atom or acetyl group)], a methyl group, a hydroxymethyl group, a 1,2-dihydroxyethyl group, a 1,2,3-trihydroxypropyl group and a 1,2,3,4-tetrahydroxybutyl group.

Preferred specific examples of ring A are,

cyclopropyl, 1-hydroxymethylcyclopropyl, 1,2-dihydroxymethyl cyclopropyl, cyclopentyl, 2-hydroxymethylcyclopentyl, 2,3-dihydroxymethylcyclopentyl, 2,3-bis(1,2-dihydroxyethyl)cyclopentyl, 2-(1,2-dihydroxyethyl)cyclopentyl, 2-(1,2,3-trihydroxypropyl)cyclopentyl, 2-(1,2,3,4-tetrahydroxybutyl)cyclopentyl,

oxirane, tetrahydrofuran, tetrahydropyrane, 1,3-dioxolane, 1,3-dioxane, 1,3-oxathiolane, 4-hydroxymethyl-1,3-dioxolane, 4,5-dihydroxymethyl-1,3-dioxolane, 4,5-bis(1,2-dihydroxyethyl)-1,3-dioxolane, 4-(1,2-dihydroxyethyl)-1,3-dioxolane, 4-(1,2,3-trihydroxypropyl)-1,3-dioxolane, 4-(1,2,3,4-tetrahydroxybutyl)-1,3-dioxolane, 4,5-diacetylaminomethyl-1,3-dioxolane, 5-hydroxy-1,3-dioxane, 5,5-dihydroxymethyl-1,3-dioxane, 5-acetylamino-1,3-dioxane, 5,5-diethoxycarbonyl-1,3-dioxane and 2,4,7,9-tetraoxaspiro[5.5]undecane,

more preferred specific examples are, 4-hydroxymethyl-1,3-dioxolane, 4,5-dihydroxymethyl-1,3-dioxolane, 4,5-bis(1,2-dihydroxyethyl)-1,3-dioxolane, 4-(1,2-dihydroxyethyl)-1,3-dioxolane, 4-(1,2,3-trihydroxypropyl)-1,3-dioxolane, 4-(1,2,3,4-tetrahydroxybutyl)-1,3-dioxolane, 4,5-diacetylaminomethyl-1,3-dioxolane, 5-hydroxy-1,3-dioxane, 5-acetylaminc-1,3-dioxane and 5,5-dihydroxymethyl-1,3-dioxane.

Ring B is a 5- to 7-membered cycloalkene group. Here, l and m, which are parameters to determine the number of members of ring B, independently from each other, are an integer of 0 to 3, and l+m is 1 to 3. The l+m being 1 to 3 represents that ring B is 5- to 7-membered. Preferably, 1 is 0, and m is an integer of 1 to 3. More preferably, it is a cyclohexynyl group in which l is 0, and m is 1.

Among the groups defined as R^1, preferred is a hydroxy group, halogen atom, C_1-C_6 alkyl group or C_1-C_6 alkoxy group, more preferred is a hydroxy group, fluorine atom, chlorine atom, methyl group, ethyl group, propyl group, methoxy group or ethoxy group, further preferred is a fluorine atom or methyl group.

The number of substitutions n, which is the number of R^1 that are substituted to ring B, is 0 to 3, preferably 0 or 1. More preferably, n is 0.

Among the groups defined as R^2, preferred is a C_1-C_6 alkyl group which may be substituted with a group selected from Substituent group β, more preferred is a C_1-C_6 alkyl group, further preferred is a C_1-C_4 alkyl group, and particularly preferred is an ethyl group.

Among the groups defined as R^3, "5- or 6-membered heteroaryl group" of "5- or 6-membered heteroaryl group which may be substituted with a group selected from Substituent group ϵ" is particularly preferably a pyrrolyl group. That is, preferably R^3 is a phenyl or pyrrolyl group which may be substituted with a group selected from Substituent group ϵ. Preferably, it is a phenyl or pyrrolyl group which may be substituted with a group selected from a halogen atom, C_1-C_{14} alkyl group and halogeno C_1-C_{14} alkyl group, more preferably a phenyl or pyrrolyl group which may be substituted with a group selected from a fluorine atom, chlorine atom, C_1-C_{10} alkyl group, halogeno C_1-C_{10} alkyl group and cyclopropyl C_1-C_{10} alkyl group, even more preferably a phenyl or pyrrolyl group which may be substituted with a group selected from a fluorine atom, chlorine atom, bromine atom, C_3-C_8 alkyl group and halogeno C_4-C_8 alkyl group, and further preferably a phenyl group which may be substituted with a group selected from a fluorine atom, chlorine atom and C_3-C_8 alkyl group.

In addition, in the case where it is substituted by a substituent, the position of substitution is preferably the 2-position or 4-position.

R^3 is, for example,

a phenyl group, halogenophenyl group, C_1-C_{14} alkylphenyl group, cyclopropyl C_1-C_{14} alkylphenyl group, C_1-C_{14} alkoxyphenyl group, C_1-C_{14} alkoxycarbonylphenyl group, carboxylphenyl group, nitrophenyl group, cyanophenyl group, halogeno C_1-C_4 alkylphenyl group, halogeno C_1-C_{14} alkoxyphenyl group, C_1-C_{14} alkanoylphenyl group, phenyl group which is substituted with a 5-membered heteroaryl group, C_1-C_{14} alkoxy-carbonyl-C_1-C_{14} alkyl-carbamoylphenyl group, 1,3-diacylguanidino-C_1-C_{14} alkylphenyl group, phenyl group which is substituted with a halogen and C_1-C_{14} alkyl, phenyl group which is substituted with a halogen and C_1-C_{14} alkoxycarbonyl, phenyl group which is substituted with a halogen and cyano, phenyl group which is substituted with a halogen and a 5-membered heteroaryl group, phenyl group which is substituted with a halogen and C_1-C_{14} alkoxy-carbonyl-C_1-C_{14} alkyl-carbamoyl,

pyrrolyl group, halogenopyrrolyl group, C_1-C_{14} alkylpyrrolyl group, cyclopropyl C_1-C_{14} alkylpyrrolyl group, C_1-C_{14} alkoxypyrrolyl group, C_1-C_{14} alkoxycarbonylpyrrolyl group, carboxylpyrrolyl group, nitropyrrolyl group, cyanopyrrolyl group, halogeno C_1-C_{14} alkylpyrrolyl group, halogeno C_1-C_{14} alkoxypyrrolyl group, C_1-C_{14} alkanoylpyrrolyl group, pyrrolyl group which is substituted with a 5-membered heteroaryl group, C_1-C_{14} alkoxy-carbonyl-C_1-C_{14} alkyl-carbamoylpyrrolyl group, 1,3-diacylguanidino-C_1-C_{14} alkylpyrrolyl group, pyrrolyl group which is substituted with a halogen and C_1-C_{14} alkyl, pyrrolyl group which is substituted with a halogen and C_1-C_{14} alkoxycarbonyl, pyrrolyl group which is substituted with a halogen and cyano, pyrrolyl group which is substituted with a halogen and a 5-membered heteroaryl group, pyrrolyl group which is substituted with a halogen and C_1-C_{14} alkoxy-carbonyl-C_1-C_{14} alkyl-carbamoyl, or the like.

Among them, specific examples are preferably,

phenyl, 2-fluorophenyl, 2-chlorophenyl, 2-bromophenyl, 2-iodophenyl, 3-fluorophenyl, 3-chlorophenyl, 4-fluorophenyl, 4-chlorophenyl, 2,3-difluorophenyl, 2,3-dichlorophenyl, 2,4-difluorophenyl, 2,4-dichlorophenyl, 2,5-difluorophenyl, 2,5-dichlorophenyl, 2,6-difluorophenyl, 2,6-dichlorophenyl, 3,4-difluorophenyl, 3,4-dichlorophenyl, 3,5-difluorophenyl, 3,5-dichlorophenyl, 2,4-dibromophenyl, 2,6-dibromophenyl, 4-chloro-2-fluorophenyl, 2-chloro-4-fluorophenyl, 4-bromo-2-fluorophenyl, 2-bromo-4-fluorophenyl, 3-chloro-4-fluorophenyl, 2-bromo-4-chlorophenyl, 5-chloro-2-fluorophenyl, 4-bromo-2-chlorophenyl, 2-chloro-6-fluorophenyl, 2,4-dimethoxyphenyl, 2,3,4-trifluorophenyl, 2,4,5-trifluorophenyl, 2,4,6-trifluorophenyl, 2-chloro-4,6-difluorophenyl, 2,6-dichloro-4-fluorophenyl, 2-bromo-6-chloro-4-fluorophenyl, 2-methylphenyl, 2-ethylphenyl, 2-(n-propyl)phenyl, 2-(n-butyl)phenyl, 2-(n-pentyl)phenyl, 2-(n-hexyl)phenyl, 2-(n-heptyl)phenyl, 2-(n-octyl)phenyl, 2-(n-nonyl)phenyl, 2-(n-decyl)phenyl, 2-(n-undecyl)phenyl, 2-(n-dodecyl)phenyl, 2-(n-tridecyl)phenyl, 2-(n-tetradecyl)phenyl, 2-ethynylphenyl, 2-isopropylphenyl, 2-t-butylphenyl, 2-sec-butylphenyl,

2-methoxyphenyl, 2-ethoxyphenyl, 2-difluoromethoxyphenyl, 2-methylsulfanylphenyl, 2-acetylphenyl, 2-benzylphenyl, 2-(morpholin-4-yl)phenyl, 2-[2-(pyridine-4-yl)ethyl]phenyl, 2-[2-(t-butoxycarbonylamino)ethyl]phenyl, 2-aminophenyl, 2,6-diisopropylphenyl, 2-chloro-4-methylphenyl, 4-fluoro-3-trifluoromethylphenyl, 4-fluoro-3-methoxyphenyl, 4-chloro-2-methoxycarbonylphenyl, 2-fluoro-4-methoxyphenyl, 4-chloro-2-methylphenyl, 2-fluoro-4-methylphenyl, 2-fluoro-5-methylphenyl, 2-chloro-4-methylphenyl, 2-chloro-6-methylphenyl, 4-t-butyl-2-chlorophenyl, 2-bromo-4-isopropylphenyl, 4-chloro-2-methoxy-5-methylphenyl, 4-fluoro-2-methylphenyl, 2-ethyl-4-fluorophenyl, 4-fluoro-2-(n-propyl)phenyl, 2-(n-butyl)-4-fluorophenyl, 4-fluoro-2-(n-pentyl)phenyl, 4-fluoro-2-(n-hexyl)phenyl, 4-fluoro-2-(n-heptyl)phenyl, 4-fluoro-2-(n-octyl)phenyl, 4-fluoro-2-(n-nonyl)phenyl, 2-(n-decyl)-4-fluorophenyl, 4-fluoro-2-(n-undecyl)phenyl, 2-(n-dodecyl)-4-fluorophenyl, 4-fluoro-2-(n-tridecyl)phenyl, 4-fluoro-2-(n-tetradecyl)phenyl, 2-trifluoromethylphenyl, 2-(2,2,2-trifluoroethyl)phenyl, 2-(3,3,3-trifluoropropyl)phenyl, 2-(4,4,4-trifluorobutyl)phenyl, 2-(5,5,5-trifluoropentyl)phenyl, 2-(6,6,6-trifluorohexyl)phenyl, 2-(7,7,7-trifluoroheptyl)phenyl, 2-(8,8,8-trifluorooctyl)phenyl, 2-(9,9,9-trifluorononyl)phenyl, 2-(10,10,10-trifluorodecyl)phenyl, 2-cyclopropylethylphenyl, 2-[3-cyclopropyl-(n-propyl)]phenyl, 2-[4-cyclopropyl-(n-butyl)]phenyl, 2-[5-cyclopropyl-(n-pentyl)]phenyl, 2-[6-cyclopropyl-(n-hexyl)]phenyl, 2-[7-cyclopropyl-(n-heptyl)]phenyl, 2-[8-cyclopropyl-(n-octyl)]phenyl, pyrrolyl, 2-fluoropyrrolyl, 2-chloropyrrolyl, 2-bromopyrrolyl, 2,5-difluoropyrrolyl, 2,5-dichloropyrrolyl, 2,5-dibromopyrrolyl, 2-chloro-5-fluoropyrrolyl, 2-methylpyrrolyl, 2-ethylpyrrolyl, 2-(n-propyl)pyrrolyl, 2-(n-butyl)pyrrolyl, 2-(n-pentyl)pyrrolyl, 2-(n-hexyl)pyrrolyl, 2-(n-heptyl)pyrrolyl, 2-(n-octyl)pyrrolyl, 2-(n-nonyl)pyrrolyl and 2-(n-decyl)pyrrolyl,

more preferably,

2-fluorophenyl, 2-chlorophenyl, 2-bromophenyl, 2-iodo phenyl, 4-fluorophenyl, 2,4-difluorophenyl, 2,4-dichlorophenyl, 2-chloro-4-fluorophenyl, 2-bromo-4-fluorophenyl, 3-chloro-4-fluorophenyl, 2-bromo-4-chlorophenyl, 2,4-dimethoxyphenyl, 2-chloro-4,6-difluorophenyl, 2,6-dichloro-4-fluorophenyl, 2-bromo-6-chloro-4-fluorophenyl, 2-methylphenyl, 2-ethylphenyl, 2-(n-propyl)phenyl, 2-(n-butyl)phenyl, 2-(n-pentyl)phenyl, 2-(n-hexyl)phenyl, 2-(n-heptyl)phenyl, 2-(n-octyl)phenyl, 2-(n-nonyl)phenyl, 2-(n-decyl)phenyl,

2-ethynylphenyl, 2-sec-butylphenyl, 2-methoxyphenyl, 2-methylsulfanylphenyl, 2-benzylphenyl, 2-[2-(t-butoxycarbonylamino)ethyl]phenyl, 4-chloro-2-methylphenyl, 2-fluoro-5-methylphenyl, 2-chloro-4-methylphenyl, 2-chloro-6-methylphenyl, 4-chloro-2-methoxy-5-methylphenyl, 4-fluoro-2-methylphenyl, 2-ethyl-4-fluorophenyl, 4-fluoro-2-(n-propyl)phenyl, 2-(n-butyl)-4-fluo-

rophenyl, 4-fluoro-2-(n-pentyl)phenyl, 4-fluoro-2-(n-hexyl)phenyl, 4-fluoro-2-(n-heptyl)phenyl, 4-fluoro-2-(n-octyl)phenyl, 4-fluoro-2-(n-nonyl)phenyl, 2-(n-decyl)-4-fluorophenyl, 2-(n-butyl)pyrrolyl, 2-(n-pentyl)pyrrolyl, 2-(n-hexyl)pyrrolyl, 2-(n-heptyl)pyrrolyl and 2-(n-octyl) pyrrolyl, and

even more preferably,

2-chlorophenyl, 2-bromophenyl, 2,4-difluorophenyl, 2-chloro-4-fluorophenyl, 2-bromo-4-fluorophenyl, 2-(n-pentyl)phenyl, 2-(n-hexyl)phenyl, 2-(n-heptyl)phenyl, 2-chloro-6-methylphenyl, 4-fluoro-2-(n-propyl)phenyl, 2-(n-butyl)-4-fluorophenyl, 4-fluoro-2-(n-pentyl)phenyl, 4-fluoro-2-(n-hexyl)phenyl, 4-fluoro-2-(n-heptyl)phenyl and 4-fluoro-2-(n-octyl)phenyl.

With respect to the "pharmacologically acceptable salts thereof", since the compound having the general formula (I) of the present invention can be converted to a salt by reaction with an acid in the case where it has a basic group such as an amino group, or by reaction with a base in the case where it has an acidic group such as a carboxyl group, salts thereof are represented.

Salts of a basic group are preferably inorganic acid salts such as hydrohalogenic acid salts including hydrochloride, hydrobromide and hydroiodide, nitrates, perchlorates, sulfates, phosphates or the like; lower alkanesulfonic acid salts such as methanesulfonate, trifluoromethanesulfonate and ethanesulfonate, arylsulfonic acid salts such as benzene sulfonate and p-toluenesulfonate, organic acid salts such as acetate, malates, fumarates, succinates, citrates, ascorbates, tartrates, oxalates, maleates or the like; and amino acid salts such as glycine salt, lysine salt, arginine salt, ornithine salt, glutamate and aspartate,

On the other hand, salts of an acidic group are preferably alkali metal salts such as sodium salt, potassium salt and lithium salt, alkaline earth metal salts such as calcium salt and magnesium salt, metal salts such as aluminum salt and iron salt; inorganic salts such as ammonium salt, amine salts including organic salts such as t-octylamine salt, dibenzylamine salt, morpholine salt, glucosamine salt, phenylglycine alkyl ester salt, ethylenediamine salt, N-methylglucamine salt, guanidine salt, diethylamine salt, triethylamine salt, dicyclohexylamine salt, N,N'-dibenzylethylenediamine salt, chloroprocaine salt, procaine salt, diethanolamine salt, N-benzylphenethylamine salt, piperazine salt, tetramethylammonium salt and tris(hydroxymethyl)aminomethane salt; and amino acid salts such as glycine salt, lysine salt, arginine salt, ornithine salt, glutamate and aspartate.

The compounds having the general formula (I) according to the present invention or pharmacologically acceptable salts thereof have an asymmetric carbon atom in their molecules, and thus stereoisomers of R configuration and S configuration exist. Each of them, or a compound with an arbitrary ratio of these, is also included in the present invention. With respect to such stereoisomers, the compound (I) can be synthesized by using an optically resolved starting compound, or a synthesized compound (I) can be optically resolved by ordinary optical resolution or separation methods if desired.

There exist optical isomers with respect to the compound having the general formula (I) according to the present invention or pharmacologically acceptable salts thereof, and each of the optical isomers and mixtures of such isomers are also included in the present invention.

When the compound having the general formula (I) and pharmacologically acceptable salts thereof are exposed to the atmosphere or are recrystallized, they may absorb moisture, resulting in cases such as the adhesion of adsorbed water and the generation of hydrates. Such hydrated compounds and salts are also included in the present invention.

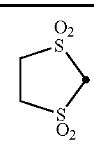
As representative compounds of the present invention, the compounds listed in the following Tables 1 to 3 can be mentioned for example, but the present invention is not limited to these compounds.

Abbreviations and "ring 1" to "ring 21" in the tables are as follows.

Ac: acetyl
Boc: butoxycarbonyl
Bn: benzyl
nBu: n-butyl
sBu: sec-butyl
tBu: tert-butyl
cBu: cyclobutylidene
ndec: n-decane
Flu: fluoren-1-yl
cPent: cyclopentylidene
cPr: cyclopropylidene
cPrl: cyclopropyl
cHept: cycloheptylidene
cHex: cyclohexylidene
dioxa: 1,3-dioxan-2-ylidene
dioxe: 1,3-dioxepan-2-ylidene
dioxo: 1,3-dioxolan-2-ylidene
dithia: 1,3-dithian-2-ylidene
dithio: 1,3-dithiolan-2-ylidene
Et: ethyl
HB: 1,2,3,4-tetrahydroxybutyl
HE: 1,2-dihydroxyethyl
nHept: n-heptyl
nHex: n-hexyl
HM: hydroxymethyl
HP: 1,2,3-trihydroxypropyl
Me: methyl
Mor: morpholino
nNon: n-nonane
O=: oxo
nOct: n-octyl
nPent: n-pentyl
Ph: phenyl
NPr: n-propyl
Pyr: pyrrolyl
Pyrd: pyridyl
S=: thioxo
oxa: 2-oxanylidene
oxathia: 1,3-oxathian-2-ylidene
oxathio: 1,3-oxathiolan-2-ylidene
oxe: 2-oxetanylidene
oxi: 2-oxiranylidene
oxo: 2-oxolanylidene
ozl: tetrahydrooxazol-2-ylidene
ozn: tetrahydro-1,3-oxadin-2-ylidene
tzl: tetrahydrothiazol-2-ylidene
tzn: tetrahydro-1,3-thiazin-2-ylidene

In the Tables, "di" indicates that there are two identical substituents, and "tri" indicates that there are three identical substituents.

ring 1:



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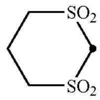
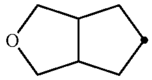
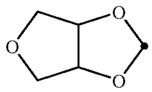
ring 2:



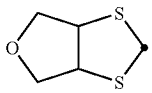
ring 3:



ring 4:



ring 5:



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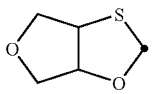
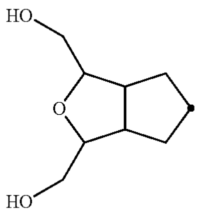
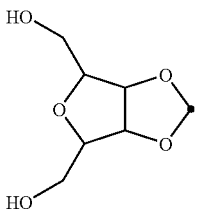


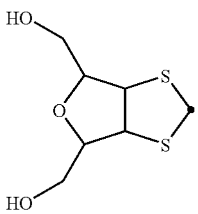
ring 7:



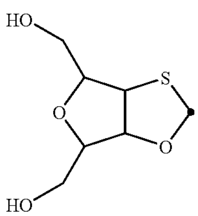
ring 8:



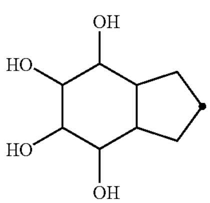
ring 9:



ring 10:



ring 11:



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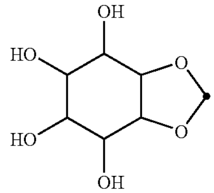
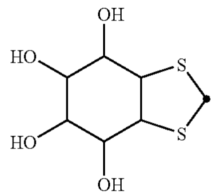
ring 12:



ring 13:



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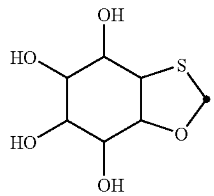

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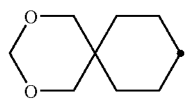
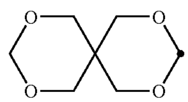


ring 16:



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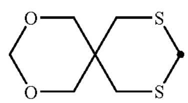

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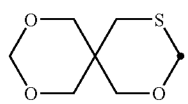

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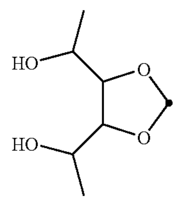
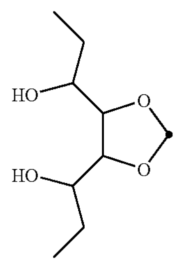


ring 20:



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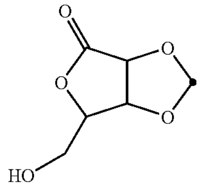
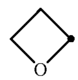
ring 21:

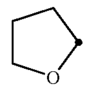


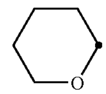
The binding position of rings 1 to 21 with ring B is the position indicated by a black dot, which is located at the right end of the aforementioned chemical structure.

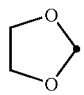
The substituents represented by the abbreviations as X and Y in Table 1, are shown below.

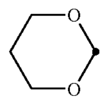

oxi


oxe


oxo


oxa


dioxo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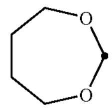
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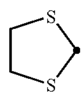
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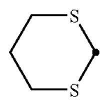
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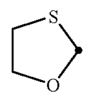
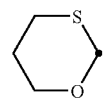

oxathio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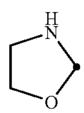
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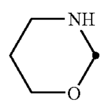
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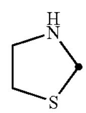
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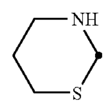
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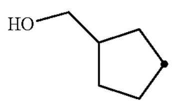
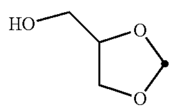

3-HM-cPent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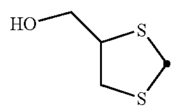
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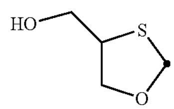
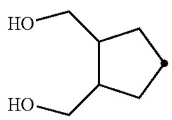
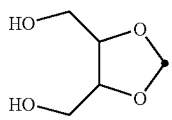
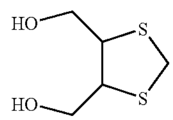
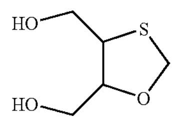

4-HM-oxathio


3,4-diHM-cPent


4,5-diHM-dioxo


4,5-diHM-dithio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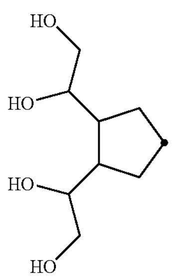
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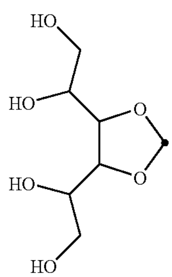
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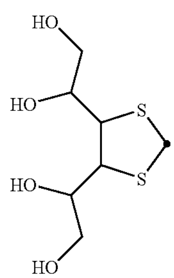
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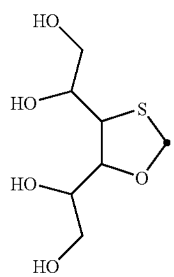
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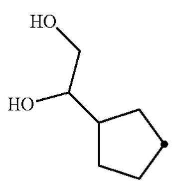
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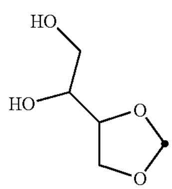
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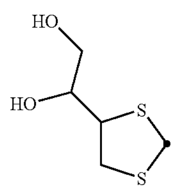
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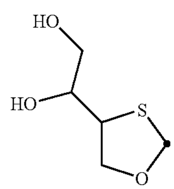
4-HE-oxathio

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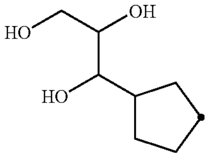
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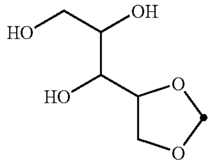
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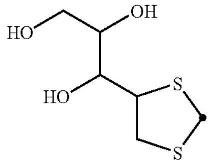
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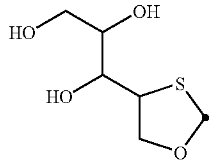
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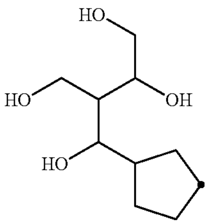
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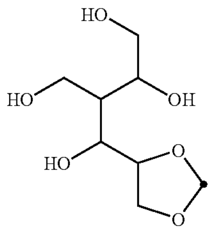
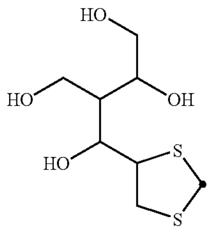
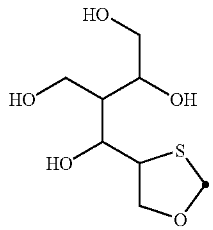
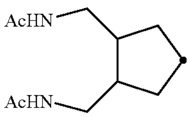
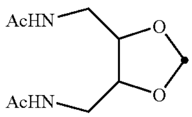
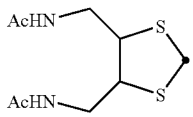

4-HB-dioxo

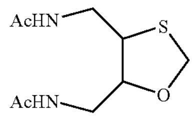

4-HB-dithio

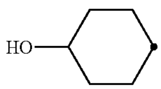

4-HB-oxathio

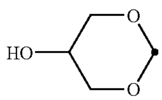

3,4-diCH_2NHAc-cPent

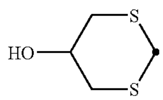

4,5-diCH_2NHAc-dioxo


4,5-diCH_2NHAc-dithio


4,5-diCH_2NHAc-oxathio


4-OH-cHex


5-OH-dioxa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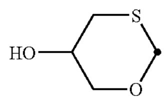
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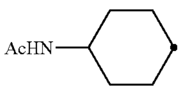
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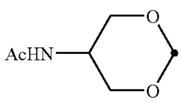
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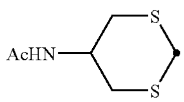
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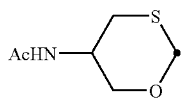
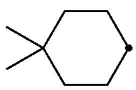
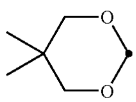
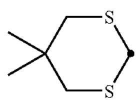
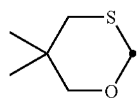

5-NHAc-oxathia


4,4-diMe-cHex


5,5-diMe-dioxa


5,5-diMe-dithia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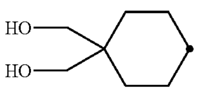
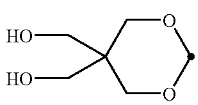

4,4-diHM-cHex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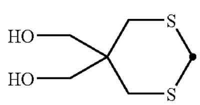
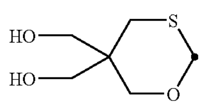
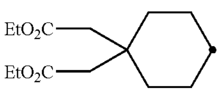
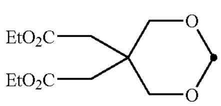
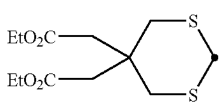

5,5-diHM-dithia


5,5-diHM-oxathia


4,4-diCO_2Et-cHex


5,5-diCO_2Et-dioxa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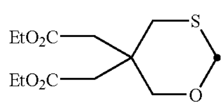
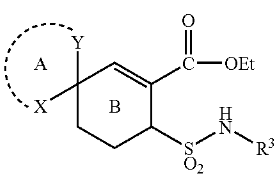
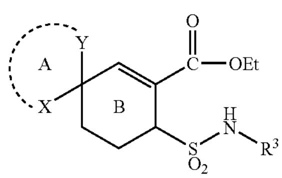

5,5-diCO_2Et-oxathia

TABLE 1



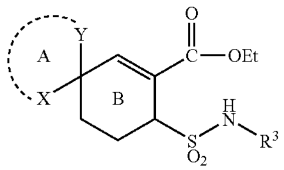
Compound No.	X, Y	R^3
1-1	O═	Ph

TABLE 1-continued



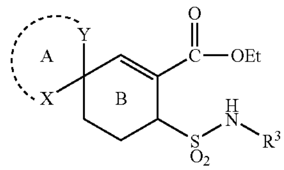
Compound No.	X, Y	R^3
1-2	S═	Ph

TABLE 1-continued



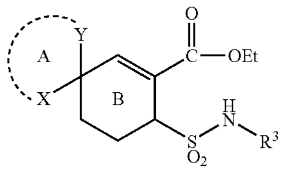
Compound No.	X, Y	R^3
1-3	cPr	Ph
1-4	cBu	Ph
1-5	cPent	Ph
1-6	cHex	Ph
1-7	cHept	Ph
1-8	oxi	Ph
1-9	oxe	Ph
1-10	oxo	Ph
1-11	oxa	Ph
1-12	dioxo	Ph
1-13	dioxa	Ph
1-14	dioxe	Ph
1-15	dithio	Ph
1-16	dithia	Ph
1-17	ring 1	Ph
1-18	ring 2	Ph
1-19	oxathio	Ph
1-20	oxathia	Ph
1-21	ozl	Ph
1-22	ozn	Ph
1-23	tzl	Ph
1-24	tzn	Ph
1-25	3-HM-cPent	Ph
1-26	4-HM-dioxo	Ph
1-27	4-HM-dithio	Ph
1-28	4-HM-oxathio	Ph
1-29	3,4-diHM-cPent	Ph
1-30	4,5-diHM-dioxo	Ph
1-31	4,5-diHM-dithio	Ph
1-32	4,5-diHM-oxathio	Ph
1-33	3,4-diHE-cPent	Ph
1-34	4,5-diHE-dioxo	Ph
1-35	4,5-diHE-dithio	Ph
1-36	4,5-diHE-oxathio	Ph
1-37	3-HE-cPent	Ph
1-38	4-HE-dioxo	Ph
1-39	4-HE-dithio	Ph
1-40	4-HE-oxathio	Ph
1-41	3-HP-cPent	Ph
1-42	4-HP-dioxo	Ph
1-43	4-HP-dithio	Ph
1-44	4-HP-oxathio	Ph
1-45	3-HB-cPent	Ph
1-46	4-HB-dioxo	Ph
1-47	4-HB-dithio	Ph
1-48	4-HB-oxathio	Ph
1-49	ring 3	Ph
1-50	ring 4	Ph
1-51	ring 5	Ph
1-52	ring 6	Ph
1-53	ring 7	Ph
1-54	ring 8	Ph
1-55	ring 9	Ph
1-56	ring 10	Ph
1-57	3,4-diCH_2NHAc-cPent	Ph
1-58	4,5-diCH_2NHAc-dioxo	Ph
1-59	4,5-diCH_2NHAc-dithio	Ph
1-60	4,5-diCH_2NHAc-oxathio	Ph
1-61	ring 11	Ph
1-62	ring 12	Ph
1-63	ring 13	Ph
1-64	ring 14	Ph
1-65	4-OH-cHex	Ph
1-66	5-OH-dioxa	Ph
1-67	5-OH-dithia	Ph
1-68	5-OH-oxathia	Ph
1-69	4-NHAc-cHex	Ph
1-70	5-NHAc-dioxa	Ph

TABLE 1-continued



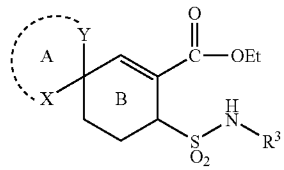
Compound No.	X, Y	R^3
1-71	5-NHAc-dithia	Ph
1-72	5-NHAc-oxathia	Ph
1-73	4,4-diMe-cHex	Ph
1-74	5,5-diMe-dioxa	Ph
1-75	5,5-diMe-dithia	Ph
1-76	5,5-diMe-oxathia	Ph
1-77	4,4-diHM-cHex	Ph
1-78	5,5-diHM-dioxa	Ph
1-79	5,5-diHM-dithia	Ph
1-80	5,5-diHM-oxathia	Ph
1-81	ring 15	Ph
1-82	ring 16	Ph
1-83	ring 17	Ph
1-84	ring 18	Ph
1-85	4,4-diCO_2Et-cHex	Ph
1-86	5,5-diCO_2Et-dioxa	Ph
1-87	5,5-diCO_2Et-dithia	Ph
1-88	5,5-diCO_2Et-oxathia	h
1-89	O═	4-F-Ph
1-90	S═	4-F-Ph
1-91	cPr	4-F-Ph
1-92	cBu	4-F-Ph
1-93	cPent	4-F-Ph
1-94	cHex	4-F-Ph
1-95	cHept	4-F-Ph
1-96	oxi	4-F-Ph
1-97	oxe	4-F-Ph
1-98	oxo	4-F-Ph
1-99	oxa	4-F-Ph
1-100	dioxo	4-F-Ph
1-101	dioxa	4-F-Ph
1-102	dioxe	4-F-Ph
1-103	dithio	4-F-Ph
1-104	dithia	4-F-Ph
1-105	ring 1	4-F-Ph
1-106	ring 2	4-F-Ph
1-107	oxathio	4-F-Ph
1-108	oxathia	4-F-Ph
1-109	ozl	4-F-Ph
1-110	ozn	4-F-Ph
1-111	tzl	4-F-Ph
1-112	tzn	4-F-Ph
1-113	3-HM-cPent	4-F-Ph
1-114	4-HM-dioxo	4-F-Ph
1-115	4-HM-dithio	4-F-Ph
1-116	4-HM-oxathio	4-F-Ph
1-117	3,4-diHM-cPent	4-F-Ph
1-118	4,5-diHM-dioxo	4-F-Ph
1-119	4,5-diHM-dithio	4-F-Ph
1-120	4,5-diHM-oxathio	4-F-Ph
1-121	3,4-diHE-cPent	4-F-Ph
1-122	4,5-diHE-diaxo	4-F-Ph
1-123	4,5-diHE-dithio	4-F-Ph
1-124	4,5-diHE-oxathio	4-F-Ph
1-125	3-HE-cPent	4-F-Ph
1-126	4-HE-dioxo	4-F-Ph
1-127	4-HE-dithio	4-F-Ph
1-128	4-HE-oxathio	4-F-Ph
1-129	3-HP-cPent	4-F-Ph
1-130	4-HP-dioxo	4-F-Ph
1-131	4-HP-dithio	4-F-Ph
1-132	4-HP-oxathio	4-F-Ph
1-133	3-HB-cPent	4-F-Ph
1-134	4-HB-dioxo	4-F-Ph
1-135	4-HB-dithio	4-F-Ph
1-136	4-HB-oxathio	4-F-Ph
1-137	ring 3	4-F-Ph
1-138	ring 4	4-F-Ph

TABLE 1-continued



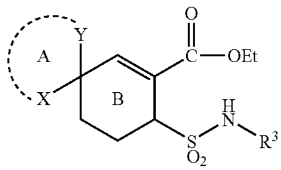
Compound No.	X, Y	R^3
1-139	ring 5	4-F-Ph
1-140	ring 6	4-F-Ph
1-141	ring 7	4-F-Ph
1-142	ring 8	4-F-Ph
1-143	ring 9	4-F-Ph
1-144	ring 10	4-F-Ph
1-145	3,4-diCH_2NHAc-cPent	4-F-Ph
1-146	4,5-diCH_2NHAc-dioxo	4-F-Ph
1-147	4,5-diCH_2NHAc-dithio	4-F-Ph
1-148	4,5-diCH_2NHAc-oxathio	4-F-Ph
1-149	ring 11	4-F-Ph
1-150	ring 12	4-F-Ph
1-151	ring 13	4-F-Ph
1-152	ring 14	4-F-Ph
1-153	4-OH-cHex	4-F-Ph
1-154	5-OH-dioxa	4-F-Ph
1-155	5-OH-dithia	4-F-Ph
1-156	5-OH-oxathia	4-F-Ph
1-157	4-NHAc-cHex	4-F-Ph
1-158	5-NHAc-dioxa	4-F-Ph
1-159	5-NHAc-dithia	4-F-Ph
1-160	5-NHAc-oxathia	4-F-Ph
1-161	4,4-diMe-cHex	4-F-Ph
1-162	5,5-diMe-dioxa	4-F-Ph
1-163	5,5-diMe-dithia	4-F-Ph
1-164	5,5-diMe-oxathia	4-F-Ph
1-165	4,4-diHM-cHex	4-F-Ph
1-166	5,5-diHM-dioxa	4-F-Ph
1-167	5,5-diHM-dithia	4-F-Ph
1-168	5,5-diHM-oxathia	4-F-Ph
1-169	ring 15	4-F-Ph
1-170	ring 16	4-F-Ph
1-171	ring 17	4-F-Ph
1-172	ring 18	4-F-Ph
1-173	4,4-diCO_2Et-cHex	4-F-Ph
1-174	5,5-diCO_2Et-dioxa	4-F-Ph
1-175	5,5-diCO_2Et-dithia	4-F-Ph
1-176	5,5-diCO_2Et-oxathia	4-F-Ph
1-177	O=	2-Cl-Ph
1-178	S=	2-Cl-Ph
1-179	cPr	2-Cl-Ph
1-180	cBn	2-Cl-Ph
1-181	cPent	2-Cl-Ph
1-182	cHex	2-Cl-Ph
1-183	cHept	2-Cl-Ph
1-184	oxi	2-Cl-Ph
1-185	oxe	2-Cl-Ph
1-186	oxo	2-Cl-Ph
1-187	oxa	2-Cl-Ph
1-188	dioxo	2-Cl-Ph
1-189	dioxa	2-Cl-Ph
1-190	dioxe	2-Cl-Ph
1-191	dithio	2-Cl-Ph
1-192	dithia	2-Cl-Ph
1-193	ring 1	2-Cl-Ph
1-194	ring 2	2-Cl-Ph
1-195	oxathio	2-Cl-Ph
1-196	oxathia	2-Cl-Ph
1-197	ozl	2-Cl-Ph
1-198	ozn	2-Cl-Ph
1-199	tzl	2-Cl-Ph
1-200	tzn	2-Cl-Ph
1-201	3-HM-cPent	2-Cl-Ph
1-202	4-HM-dioxo	2-Cl-Ph
1-203	4-HM-dithio	2-Cl-Ph
1-204	4-HM-oxathio	2-Cl-Ph
1-205	3,4-diHM-cPent	2-Cl-Ph
1-206	4,5-diHM-dioxo	2-Cl-Ph

TABLE 1-continued



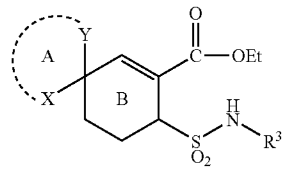
Compound No.	X, Y	R^3
1-207	4,5-diHM-dithio	2-Cl-Ph
1-208	4,5-diHM-oxathio	2-Cl-Ph
1-209	3,4-diHE-cPent	2-Cl-Ph
1-210	4,5-diHE-dioxo	2-Cl-Ph
1-211	4,5-diHE-dithio	2-Cl-Ph
1-212	4,5-diHE-oxathio	2-Cl-Ph
1-213	3-HE-cPent	2-Cl-Ph
1-214	4-HE-dioxo	2-Cl-Ph
1-215	4-HE-dithio	2-Cl-Ph
1-216	4-HE-oxathio	2-Cl-Ph
1-217	3-HP-cPent	2-Cl-Ph
1-218	4-HP-dioxo	2-Cl-Ph
1-219	4-HP-dithio	2-Cl-Ph
1-220	4-HP-oxathio	2-Cl-Ph
1-221	3-HB-cPent	2-Cl-Ph
1-222	4-HB-dioxo	2-Cl-Ph
1-223	4-HB-dithio	2-Cl-Ph
1-224	4-HB-oxathio	2-Cl-Ph
1-225	ring 3	2-Cl-Ph
1-226	ring 4	2-Cl-Ph
1-227	ring 5	2-Cl-Ph
1-228	ring 6	2-Cl-Ph
1-229	ring 7	2-Cl-Ph
1-230	ring 8	2-Cl-Ph
1-231	ring 9	2-Cl-Ph
1-232	ring 10	2-Cl-Ph
1-233	3,4-diCH_2NHAc-cPent	2-Cl-Ph
1-234	4,5-diCH_2NHAc-dioxo	2-Cl-Ph
1-235	4,5-diCH_2NHAc-dithio	2-Cl-Ph
1-236	4,5-diCH_2NHAc-oxathio	2-Cl-Ph
1-237	ring 11	2-Cl-Ph
1-238	ring 12	2-Cl-Ph
1-239	ring 13	2-Cl-Ph
1-240	ring 14	2-Cl-Ph
1-241	4-OH-cHex	2-Cl-Ph
1-242	5-OH-dioxa	2-Cl-Ph
1-243	5-OH-dithia	2-Cl-Ph
1-244	5-OH-oxathia	2-Cl-Ph
1-245	4-NHAc-cHex	2-Cl-Ph
1-246	5-NHAc-dioxa	2-Cl-Ph
1-247	5-NHAc-dithia	2-Cl-Ph
1-248	5-NHAc-oxathia	2-Cl-Ph
1-249	4,4-diMe-cHex	2-Cl-Ph
1-250	5,5-diMe-dioxa	2-Cl-Ph
1-251	5,5-diMe-dithia	2-Cl-Ph
1-252	5,5-diMe-oxathia	2-Cl-Ph
1-253	4,4-diHM-cHex	2-Cl-Ph
1-254	5,5-diHM-dioxa	2-Cl-Ph
1-255	5,5-diHM-dithia	2-Cl-Ph
1-256	5,5-diHM-oxathia	2-Cl-Ph
1-257	ring 15	2-Cl-Ph
1-258	ring 16	2-Cl-Ph
1-259	ring 17	2-Cl-Ph
1-260	ring 18	2-Cl-Ph
1-261	4,4-diCO_2Et-cHex	2-Cl-Ph
1-262	5,5-diCO_2Et-dioxa	2-Cl-Ph
1-263	5,5-diCO_2Et-dithia	2-Cl-Ph
1-264	5,5-diCO_2Et-oxathia	2-Cl-Ph
1-265	O=	2,4-diF-Ph
1-266	S=	2,4-diF-Ph
1-267	cPr	2,4-diF-Ph
1-268	cBu	2,4-diF-Ph
1-269	cPent	2,4-diF-Ph
1-270	cHex	2,4-diF-Ph
1-271	cHept	2,4-diF-Ph
1-272	oxi	2,4-diF-Ph
1-273	oxe	2,4-diF-Ph
1-274	oxo	2,4-diF-Ph

TABLE 1-continued



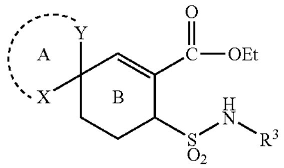
Compound No.	X, Y	R^3
1-275	oxa	2,4-diF-Ph
1-276	dioxo	2,4-diF-Ph
1-277	dioxa	2,4-diF-Ph
1-278	dioxe	2,4-diF-Ph
1-279	dithio	2,4-diF-Ph
1-280	dithia	2,4-diF-Ph
1-281	ring 1	2,4-diF-Ph
1-282	ring 2	2,4-diF-Ph
1-283	oxathio	2,4-diF-Ph
1-284	oxathia	2,4-diF-Ph
1-285	ozl	2,4-diF-Ph
1-286	ozn	2,4-diF-Ph
1-287	tzl	2,4-diF-Ph
1-288	tzn	2,4-diF-Ph
1-289	3-HM-cPent	2,4-diF-Ph
1-290	4-HM-dioxo	2,4-diF-Ph
1-291	4-HM-dithio	2,4-diF-Ph
1-292	4-HM-oxathio	2,4-diF-Ph
1-293	3,4-diHM-cPent	2,4-diF-Ph
1-294	4,5-diHM-dioxo	2,4-diF-Ph
1-295	4,5-diHM-dithio	2,4-diF-Ph
1-296	4,5-diHM-oxathio	2,4-diF-Ph
1-297	3,4-diHE-cPent	2,4-diF-Ph
1-298	4,5-diHE-dioxo	2,4-diF-Ph
1-299	4,5-diHE-dithio	2,4-diF-Ph
1-300	4,5-diHE-oxathio	2,4-diF-Ph
1-301	3-HE-cPent	2,4-diF-Ph
1-302	4-HE-dioxo	2,4-diF-Ph
1-303	4-HE-dithio	2,4-diF-Ph
1-304	4-HE-oxathio	2,4-diF-Ph
1-305	3-HP-cPent	2,4-diF-Ph
1-306	4-HP-dioxo	2,4-diF-Ph
1-307	4-HP-dithio	2,4-diF-Ph
1-308	4-HP-oxathio	2,4-diF-Ph
1-309	3-HB-cPent	2,4-diF-Ph
1-310	4-HB-dioxo	2,4-diF-Ph
1-311	4-HB-dithio	2,4-diF-Ph
1-312	4-HB-oxathio	2,4-diF-Ph
1-313	ring 3	2,4-diF-Ph
1-314	ring 4	2,4-diF-Ph
1-315	ring 5	2,4-diF-Ph
1-316	ring 6	2,4-diF-Ph
1-317	ring 7	2,4-diF-Ph
1-318	ring 8	2,4-diF-Ph
1-319	ring 9	2,4-diF-Ph
1-320	ring 10	2,4-diF-Ph
1-321	3,4-diCH_2NHAc-cPent	2,4-diF-Ph
1-322	4,5-diCH_2NHAc-dioxo	2,4-diF-Ph
1-323	4,5-diCH_2NHAc-dithio	2,4-diF-Ph
1-324	4,5-diCH_2NHAc-oxathio	2,4-diF-Ph
1-325	ring 11	2,4-diF-Ph
1-326	ring 12	2,4-diF-Ph
1-327	ring 13	2,4-diF-Ph
1-328	ring 14	2,4-diF-Ph
1-329	4-OH-cHex	2,4-diF-Ph
1-330	5-OH-dioxa	2,4-diF-Ph
1-331	5-OH-dithia	2,4-diF-Ph
1-332	5-OH-oxathia	2,4-diF-Ph
1-333	4-NHAc-cHex	2,4-diF-Ph
1-334	5-NHAc-dioxa	2,4-diF-Ph
1-335	5-NHAc-dithia	2,4-diF-Ph
1-336	5-NHAc-oxathia	2,4-diF-Ph
1-337	4,4-diMe-cHex	2,4-diF-Ph
1-338	5,5-diMe-dioxa	2,4-diF-Ph
1-339	5,5-diMe-dithia	2,4-diF-Ph
1-340	5,5-diMe-oxathia	2,4-diF-Ph
1-341	4,4-diHM-cHex	2,4-diF-Ph
1-342	5,5-diHM-dioxa	2,4-diF-Ph

TABLE 1-continued



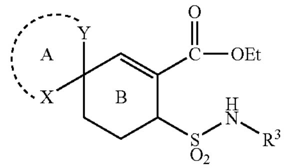
Compound No.	X, Y	R^3
1-343	5,5-diHM-dithia	2,4-diF-Ph
1-344	5,5-diHM-oxathia	2,4-diF-Ph
1-345	ring 15	2,4-diF-Ph
1-346	ring 16	2,4-diF-Ph
1-347	ring 17	2,4-diF-Ph
1-348	ring 18	2,4-diF-Ph
1-349	4,4-diCO_2Et-cHex	2,4-diF-Ph
1-350	5,5-diCO_2Et-dioxa	2,4-diF-Ph
1-351	5,5-diCO_2Et-dithia	2,4-diF-Ph
1-352	5,5-diCO_2Et-oxathia	2,4-diF-Ph
1-353	O=	2-Cl-4-F-Ph
1-354	S=	2-Cl-4-F-Ph
1-355	cPr	2-Cl-4-F-Ph
1-356	cBu	2-Cl-4-F-Ph
1-357	cPent	2-Cl-4-F-Ph
1-358	cHex	2-Cl-4-F-Ph
1-359	cHept	2-Cl-4-F-Ph
1-360	oxi	2-Cl-4-F-Ph
1-361	oxe	2-Cl-4-F-Ph
1-362	oxo	2-Cl-4-F-Ph
1-363	oxa	2-Cl-4-F-Ph
1-364	dioxo	2-Cl-4-F-Ph
1-365	dioxa	2-Cl-4-F-Ph
1-366	dioxe	2-Cl-4-F-Ph
1-367	dithio	2-Cl-4-F-Ph
1-368	dithia	2-Cl-4-F-Ph
1-369	ring 1	2-Cl-4-F-Ph
1-370	ring 2	2-Cl-4-F-Ph
1-371	oxathio	2-Cl-4-F-Ph
1-372	oxathia	2-Cl-4-F-Ph
1-373	ozl	2-Cl-4-F-Ph
1-374	ozn	2-Cl-4-F-Ph
1-375	tzl	2-Cl-4-F-Ph
1-376	tzn	2-Cl-4-F-Ph
1-377	3-HM-cPent	2-Cl-4-F-Ph
1-378	4-HM-dioxo	2-Cl-4-F-Ph
1-379	4-HM-dithio	2-Cl-4-F-Ph
1-380	4-HM-oxathio	2-Cl-4-F-Ph
1-381	3,4-diHM-cPent	2-Cl-4-F-Ph
1-382	4,5-diHM-dioxo	2-Cl-4-F-Ph
1-383	4,5-diHM-dithio	2-Cl-4-F-Ph
1-384	4,5-diHM-oxathio	2-Cl-4-F-Ph
1-385	3,4-diHE-cPent	2-Cl-4-F-Ph
1-386	4,5-diHE-dioxo	2-Cl-4-F-Ph
1-387	4,5-diHE-dithio	2-Cl-4-F-Ph
1-388	4,5-diHE-oxathio	2-Cl-4-F-Ph
1-389	3-HE-cPent	2-Cl-4-F-Ph
1-390	4-HE-dioxo	2-Cl-4-F-Ph
1-391	4-HE-dithio	2-Cl-4-F-Ph
1-392	4-HE-oxathio	2-Cl-4-F-Ph
1-393	3-HP-cPent	2-Cl-4-F-Ph
1-394	4-HP-dioxo	2-Cl-4-F-Ph
1-395	4-HP-dithio	2-Cl-4-F-Ph
1-396	4-HP-oxathio	2-Cl-4-F-Ph
1-397	3-HB-cPent	2-Cl-4-F-Ph
1-398	4-HB-dioxo	2-Cl-4-F-Ph
1-399	4-HB-dithio	2-Cl-4-F-Ph
1-400	4-HB-oxathio	2-Cl-4-F-Ph
1-401	ring 3	2-Cl-4-F-Ph
1-402	ring 4	2-Cl-4-F-Ph
1-403	ring 5	2-Cl-4-F-Ph
1-404	ring 6	2-Cl-4-F-Ph
1-405	ring 7	2-Cl-4-F-Ph
1-406	ring 8	2-Cl-4-F-Ph
1-407	ring 9	2-Cl-4-F-Ph
1-408	ring 10	2-Cl-4-F-Ph
1-409	3,4-diCH_2NHAc-cPent	2-Cl-4-F-Ph
1-410	4,5-diCH_2NHAc-dioxo	2-Cl-4-F-Ph

TABLE 1-continued



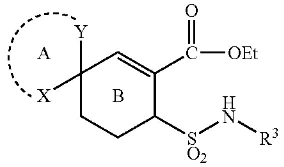
Compound No.	X, Y	R^3
1-411	4,5-diCH$_2$NHAc-dithio	2-Cl-4-F-Ph
1-412	4,5-diCH$_2$NHAc-oxathio	2-Cl-4-F-Ph
1-413	ring 11	2-Cl-4-F-Ph
1-414	ring 12	2-Cl-4-F-Ph
1-415	ring 13	2-Cl-4-F-Ph
1-416	ring 14	2-Cl-4-F-Ph
1-417	4-OH-cHex	2-Cl-4-F-Ph
1-418	5-OH-dioxa	2-Cl-4-F-Ph
1-419	5-OH-dithia	2-Cl-4-F-Ph
1-420	5-OH-oxathia	2-Cl-4-F-Ph
1-421	4-NHAc-cHex	2-Cl-4-F-Ph
1-422	5-NHAc-dioxa	2-Cl-4-F-Ph
1-423	5-NHAc-dithia	2-Cl-4-F-Ph
1-424	5-NHAc-oxathia	2-Cl-4-F-Ph
1-425	4,4-diMe-cHex	2-Cl-4-F-Ph
1-426	5,5-diMe-dioxa	2-Cl-4-F-Ph
1-427	5,5-diMe-dithia	2-Cl-4-F-Ph
1-428	5,5-diMe-oxathia	2-Cl-4-F-Ph
1-429	4,4-diHM-cHex	2-Cl-4-F-Ph
1-430	5,5-diHM-dioxa	2-Cl-4-F-Ph
1-431	5,5-diHM-dithia	2-Cl-4-F-Ph
1-432	5,5-diHM-oxathia	2-Cl-4-F-Ph
1-433	ring 15	2-Cl-4-F-Ph
1-434	ring 16	2-Cl-4-F-Ph
1-435	ring 17	2-Cl-4-F-Ph
1-436	ring 18	2-Cl-4-F-Fh
1-437	4,4-diCO$_2$Et-cHex	2-Cl-4-F-Ph
1-438	5,5-diCO$_2$Et-dioxa	2-Cl-4-F-Ph
1-439	5,5-diCO$_2$Et-dithia	2-Cl-4-F-Ph
1-440	5,5-diCO$_2$Et-oxathia	2-Cl-4-F-Fh
1-441	O═	2-Cl-4-Me-Ph
1-442	S═	2-Cl-4-Me-Ph
1-443	cPr	2-Cl-4-Me-Ph
1-444	cBu	2-Cl-4-Me-Ph
1-445	cPent	2-Cl-4-Me-Ph
1-446	cHex	2-Cl-4-Me-Ph
1-447	cHept	2-Cl-4-Me-Ph
1-448	oxi	2-Cl-4-Me-Ph
1-449	oxe	2-Cl-4-Me-Ph
1-450	oxo	2-Cl-4-Me-Ph
1-451	oxa	2-Cl-4-Me-Ph
1-452	dioxo	2-Cl-4-Me-Ph
1-453	dioxa	2-Cl-4-Me-Ph
1-454	dioxe	2-Cl-4-Me-Ph
1-455	dithio	2-Cl-4-Me-Ph
1-456	dithia	2-Cl-4-Me-Ph
1-457	ring 1	2-Cl-4-Me-Ph
1-458	ring 2	2-Cl-4-Me-Ph
1-459	oxathio	2-Cl-4-Me-Ph
1-460	oxathia	2-Cl-4-Me-Ph
1-461	ozl	2-Cl-4-Me-Ph
1-462	ozn	2-Cl-4-Me-Ph
1-463	tzl	2-Cl-4-Me-Ph
1-464	tzn	2-Cl-4-Me-Ph
1-465	3-HM-cPent	2-Cl-4-Me-Ph
1-466	4-HM-dioxo	2-Cl-4-Me-Ph
1-467	4-HM-dithio	2-Cl-4-Me-Ph
1-468	4-HM-oxathio	2-Cl-4-Me-Ph
1-469	3,4-diHM-cPent	2-Cl-4-Me-Ph
1-470	4,5-diHM-dioxo	2-Cl-4-Me-Ph
1-471	4,5-diHM-dithio	2-Cl-4-Me-Ph
1-472	4,5-diHM-oxathio	2-Cl-4-Me-Ph
1-473	3,4-diHE-cPent	2-Cl-4-Me-Ph
1-474	4,5-diHE-dioxo	2-Cl-4-Me-Ph
1-475	4,5-diHE-dithio	2-Cl-4-Me-Ph
1-476	4,5-diHE-oxathio	2-Cl-4-Me-Ph
1-477	3-HE-cPent	2-Cl-4-Me-Ph
1-478	4-HE-dioxo	2-Cl-4-Me-Ph

TABLE 1-continued



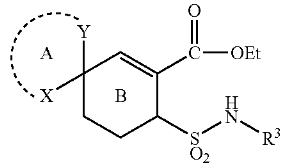
Compound No.	X, Y	R^3
1-479	4-HE-dithio	2-Cl-4-Me-Ph
1-480	4-HE-oxathio	2-Cl-4-Me-Ph
1-481	3-HP-cPent	2-Cl-4-Me-Ph
1-482	4-HP-dioxo	2-Cl-4-Me-Ph
1-483	4-HP-dithio	2-Cl-4-Me-Ph
1-484	4-HP-oxathio	2-Cl-4-Me-Ph
1-485	3-HB-cPent	2-Cl-4-Me-Ph
1-486	4-HB-dioxo	2-Cl-4-Me-Ph
1-487	4-HB-dithio	2-Cl-4-Me-Ph
1-488	4-HB-oxathio	2-Cl-4-Me-Ph
1-489	ring 3	2-Cl-4-Me-Ph
1-490	ring 4	2-Cl-4-Me-Ph
1-491	ring 5	2-Cl-4-Me-Ph
1-492	ring 6	2-Cl-4-Me-Ph
1-493	ring 7	2-Cl-4-Me-Ph
1-494	ring 8	2-Cl-4-Me-Ph
1-495	ring 9	2-Cl-4-Me-Ph
1-496	ring 10	2-Cl-4-Me-Ph
1-497	3,4-diCH$_2$NHAc-cPent	2-Cl-4-Me-Ph
1-498	4,5-diCH$_2$NHAc-dioxo	2-Cl-4-Me-Ph
1-499	4,5-diCH$_2$NHAc-dithio	2-Cl-4-Me-Ph
1-500	4,5-diCH$_2$NHAc-oxathio	2-Cl-4-Me-Ph
1-501	ring 11	2-Cl-4-Me-Ph
1-502	ring 12	2-Cl-4-Me-Ph
1-503	ring 13	2-Cl-4-Me-Ph
1-504	ring 14	2-Cl-4-Me-Ph
1-505	4-OH-cHex	2-Cl-4-Me-Ph
1-506	5-OH-dioxa	2-Cl-4-Me-Ph
1-507	5-OH-dithia	2-Cl-4-Me-Ph
1-508	5-OH-oxathia	2-Cl-4-Me-Ph
1-509	4-NHAc-cHex	2-Cl-4-Me-Ph
1-510	5-NHAc-dioxa	2-Cl-4-Me-Ph
1-511	5-NHAc-dithia	2-Cl-4-Me-Ph
1-512	5-NHAc-oxathia	2-Cl-4-Me-Ph
1-513	4,4-diMe-cHex	2-Cl-4-Me-Ph
1-514	5,5-diMe-dioxa	2-Cl-4-Me-Ph
1-515	5,5-diMe-dithia	2-Cl-4-Me-Ph
1-516	5,5-diMe-oxathia	2-Cl-4-Me-Ph
1-517	4,4-diHM-cHex	2-Cl-4-Me-Ph
1-518	5,5-diHM-dioxa	2-Cl-4-Me-Ph
1-519	5,5-diHM-dithia	2-Cl-4-Me-Ph
1-520	5,5-diHM-oxathia	2-Cl-4-Me-Ph
1-521	ring 15	2-Cl-4-Me-Ph
1-522	ring 16	2-Cl-4-Me-Ph
1-523	ring 17	2-Cl-4-Me-Ph
1-524	ring 18	2-Cl-4-Me-Ph
1-525	4,4-diCO$_2$Et-cHex	2-Cl-4-Me-Ph
1-526	5,5-diCO$_2$Et-dioxa	2-Cl-4-Me-Ph
1-527	5,5-diCO$_2$Et-dithia	2-Cl-4-Me-Ph
1-528	5,5-diCO$_2$Et-oxathia	2-Cl-4-Me-Ph
1-529	O═	2-nBu-Ph
1-530	S═	2-nBu-Ph
1-531	cPr	2-nBu-Ph
1-532	cBu	2-nBu-Ph
1-533	cPent	2-nBu-Ph
1-534	cHex	2-nBu-Ph
1-535	cHept	2-nBu-Ph
1-536	oxi	2-nBu-Ph
1-537	oxe	2-nBu-Ph
1-538	oxo	2-nBu-Ph
1-539	oxa	2-nBu-Ph
1-540	dioxo	2-nBu-Ph
1-541	dioxa	2-nBu-Ph
1-542	dioxe	2-nBu-Ph
1-543	dithio	2-nBu-Ph
1-544	dithia	2-nBu-Ph
1-545	ring 1	2-nBu-Ph
1-546	ring 2	2-nBu-Ph

TABLE 1-continued



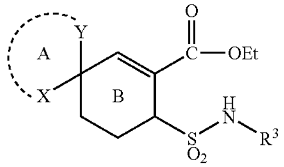
Compound No.	X, Y	R^3
1-547	oxathio	2-nBu-Ph
1-548	oxathia	2-nBu-Ph
1-549	ozl	2-nBu-Ph
1-550	ozn	2-nBu-Ph
1-551	tzl	2-nBu-Ph
1-552	tzn	2-nBu-Ph
1-553	3-HM-cPent	2-nBu-Ph
1-554	4-HM-dioxo	2-nBu-Ph
1-555	4-HM-dithio	2-nBu-Ph
1-556	4-HM-oxathio	2-nBu-Ph
1-557	3,4-diHM-cPent	2-nBu-Ph
1-558	4,5-diHM-dioxo	2-nBu-Ph
1-559	4,5-diHM-dithio	2-nBu-Ph
1-560	4,5-diHM-oxathio	2-nBu-Ph
1-561	3,4-diHE-cPent	2-nBu-Ph
1-562	4,5-diHE-dioxo	2-nBu-Ph
1-563	4,5-diHE-dithio	2-nBu-Ph
1-564	4,5-diHE-oxathio	2-nBu-Ph
1-565	3-HE-cPent	2-nBu-Ph
1-566	4-HE-dioxo	2-nBu-Ph
1-567	4-HE-dithio	2-nBu-Ph
1-568	4-HE-oxathio	2-nBu-Ph
1-569	3-HP-cPent	2-nBu-Ph
1-570	4-HP-dioxo	2-nBu-Ph
1-571	4-HP-dithio	2-nBu-Ph
1-572	4-HP-oxathio	2-nBu-Ph
1-573	3-HB-cPent	2-nBu-Ph
1-574	4-HB-dioxo	2-nBu-Ph
1-575	4-HB-dithio	2-nBu-Ph
1-576	4-HB-oxathio	2-nBu-Ph
1-577	ring 3	2-nBu-Ph
1-578	ring 4	2-nBu-Ph
1-579	ring 5	2-nBu-Ph
1-580	ring 6	2-nBu-Ph
1-581	ring 7	2-nBu-Ph
1-582	ring 8	2-nBu-Ph
1-583	ring 9	2-nBu-Ph
1-584	ring 10	2-nBu-Ph
1-585	3,4-diCH_2NHAc-cPent	2-nBu-Ph
1-586	4,5-diCH_2NHAc-dioxo	2-nBu-Ph
1-587	4,5-diCH_2NHAc-dithio	2-nBu-Ph
1-588	4,5-diCH_2NHAc-oxathio	2-nBu-Ph
1-589	ring 11	2-nBu-Ph
1-590	ring 12	2-nBu-Ph
1-591	ring 13	2-nBu-Ph
1-592	ring 14	2-nBu-Ph
1-593	4-OH-cHex	2-nBu-Ph
1-594	5-OH-dioxa	2-nBu-Ph
1-595	5-OH-dithia	2-nBu-Ph
1-596	5-OH-oxathia	2-nBu-Ph
1-597	4-NHAc-cHex	2-nBu-Ph
1-598	5-NHAc-dioxa	2-nBu-Ph
1-599	5-NHAc-dithia	2-nBu-Ph
1-600	5-NHAc-oxathia	2-nBu-Ph
1-601	4,4-diMe-cHex	2-nBu-Ph
1-602	5,5-diMe-dioxa	2-nBu-Ph
1-603	5,5-diMe-dithia	2-nBu-Ph
1-604	5,5-diMe-oxathia	2-nBu-Ph
1-605	4,4-diHM-cHex	2-nBu-Ph
1-606	5,5-diHM-dioxa	2-nBu-Ph
1-607	5,5-diHM-dithia	2-nBu-Ph
1-608	5,5-diHM-oxathia	2-nBu-Ph
1-609	ring 15	2-nBu-Ph
1-610	ring 16	2-nBu-Ph
1-611	ring 17	2-nBu-Ph
1-612	ring 18	2-nBu-Ph
1-612	4,4-diCO_2Et-cHex	2-nBu-Ph
1-614	5,5-diCO_2Et-dioxa	2-nBu-Ph

TABLE 1-continued



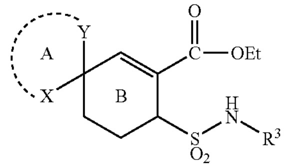
Compound No.	X, Y	R^3
1-615	5,5-diCO_2Et-dithia	2-nBu-Ph
1-616	5,5-diCO_2Et-oxathia	2-nBu-Ph
1-617	O═	2-nBu-4-F-Ph
1-618	S═	2-nBu-4-F-Ph
1-619	cPr	2-nBu-4-F-Ph
1-620	cBu	2-nBu-4-F-Ph
1-621	cPent	2-nBu-4-F-Ph
1-622	cHex	2-nBu-4-F-Ph
1-623	cHept	2-nBu-4-F-Ph
1-624	oxi	2-nBu-4-F-Ph
1-625	oxe	2-nBu-4-F-Ph
1-626	oxo	2-nBu-4-F-Ph
1-627	oxa	2-nBu-4-F-Ph
1-628	dioxo	2-nBu-4-F-Ph
1-629	dioxa	2-nBu-4-F-Ph
1-630	dioxe	2-nBu-4-F-Ph
1-631	dithio	2-nBu-4-F-Ph
1-632	dithia	2-nBu-4-F-Ph
1-633	ring 1	2-nBu-4-F-Ph
1-634	ring 2	2-nBu-4-F-Ph
1-635	oxathio	2-nBu-4-F-Ph
1-636	oxathia	2-nBu-4-F-Ph
1-637	ozl	2-nBu-4-F-Ph
1-638	ozn	2-nBu-4-F-Ph
1-639	tzl	2-nBu-4-F-Ph
1-640	tzn	2-nBu-4-F-Ph
1-641	3-HM-cPent	2-nBu-4-F-Ph
1-642	4-HM-dioxo	2-nBu-4-F-Ph
1-643	4-HM-dithio	2-nBu-4-F-Ph
1-644	4-HM-oxathio	2-nBu-4-F-Ph
1-645	3,4-diHM-cPent	2-nBu-4-F-Ph
1-646	4,5-diHM-dioxo	2-nBu-4-F-Ph
1-647	4,5-diHM-dithio	2-nBu-4-F-Ph
1-648	4,5-diHM-oxathio	2-nBu-4-F-Ph
1-649	3,4-diHE-cPent	2-nBu-4-F-Ph
1-650	4,5-diHE-dioxo	2-nBu-4-F-Ph
1-651	4,5-diHE-dithio	2-nBu-4-F-Ph
1-652	4,5-diHE-oxathio	2-nBu-4-F-Ph
1-653	3-HE-cPent	2-nBu-4-F-Ph
1-654	4-HE-dioxo	2-nBu-4-F-Ph
1-655	4-HE-dithio	2-nBu-4-F-Ph
1-656	4-HE-oxathio	2-nBu-4-F-Ph
1-657	3-HP-cPent	2-nBu-4-F-Ph
1-658	4-HP-dioxo	2-nBu-4-F-Ph
1-659	4-HP-dithio	2-nBu-4-F-Ph
1-660	4-HP-oxathio	2-nBu-4-F-Ph
1-661	3-HB-cPent	2-nBu-4-F-Ph
1-662	4-HB-dioxo	2-nBu-4-F-Ph
1-663	4-HB-dithio	2-nBu-4-F-Ph
1-664	4-HB-oxathio	2-nBu-4-F-Ph
1-665	ring 3	2-nBu-4-F-Ph
1-666	ring 4	2-nBu-4-F-Ph
1-667	ring 5	2-nBu-4-F-Ph
1-668	ring 6	2-nBu-4-F-Ph
1-669	ring 7	2-nBu-4-F-Ph
1-670	ring 8	2-nBu-4-F-Ph
1-671	ring 9	2-nBu-4-F-Ph
1-672	ring 10	2-nBu-4-F-Ph
1-673	3,4-diCH_2NHAc-cPent	2-nBu-4-F-Ph
1-674	4,5-diCH_2NHAc-dioxo	2-nBu-4-F-Ph
1-675	4,5-diCH_2NHAc-dithio	2-nBu-4-F-Ph
1-676	4,5-diCH_2NHAc-oxathio	2-nBu-4-F-Ph
1-677	ring 11	2-nBu-4-F-Ph
1-678	ring 12	2-nBu-4-F-Ph
1-679	ring 13	2-nBu-4-F-Ph
1-680	ring 14	2-nBu-4-F-Ph
1-681	4-OH-cHex	2-nBu-4-F-Ph
1-682	5-OH-dioxa	2-nBu-4-F-Ph

TABLE 1-continued



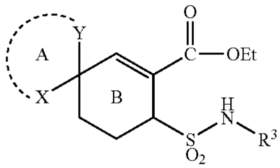
Compound No.	X, Y	R^3
1-683	5-OH-dithia	2-nBu-4-F-Ph
1-684	5-OH-oxathia	2-nBu-4-F-Ph
1-685	4-NHAc-cHex	2-nBu-4-F-Ph
1-686	5-NHAc-dioxa	2-nBu-4-F-Ph
1-687	5-NHAc-dithia	2-nBu-4-F-Ph
1-688	5-NHAc-oxathia	2-nBu-4-F-Ph
1-689	4,4-diMe-cHex	2-nBu-4-F-Ph
1-690	5,5-diMe-dioxa	2-nBu-4-F-Ph
1-691	5,5-diMe-dithia	2-nBu-4-F-Ph
1-692	5,5-diMe-oxathia	2-nBu-4-F-Ph
1-693	4,4-diHM-cHex	2-nBu-4-F-Ph
1-694	5,5-diHM-dioxa	2-nBu-4-F-Ph
1-695	5,5-diHM-dithia	2-nBu-4-F-Ph
1-696	5,5-diHM-oxathia	2-nBu-4-F-Ph
1-697	ring 15	2-nBu-4-F-Ph
1-698	ring 16	2-nBu-4-F-Ph
1-699	ring 17	2-nBu-4-F-Ph
1-700	ring 18	2-nBu-4-F-Ph
1-701	4,4-diCO$_2$Et-cHex	2-nBu-4-F-Ph
1-702	5,5-diCO$_2$Et-dioxa	2-nBu-4-F-Ph
1-703	5,5-diCO$_2$Et-dithia	2-nBu-4-F-Ph
1-704	5,5-diCO$_2$Et-oxathia	2-nBu-4-F-Ph
1-705	O=	2-nHex-Ph
1-706	S=	2-nHex-Ph
1-707	cPr	2-nHex-Ph
1-708	cBu	2-nHex-Ph
1-709	cPent	2-nHex-Ph
1-710	cHex	2-nHex-Ph
1-711	cHept	2-nHex-Ph
1-712	oxi	2-nHex-Ph
1-713	oxe	2-nHex-Ph
1-714	oxo	2-nHex-Ph
1-715	oxa	2-nHex-Ph
1-716	dioxo	2-nHex-Ph
1-717	dioxa	2-nHex-Ph
1-718	dioxe	2-nHex-Ph
1-719	dithio	2-nHex-Ph
1-720	dithia	2-nHex-Ph
1-721	ring 1	2-nHex-Ph
1-722	ring 2	2-nHex-Ph
1-723	oxathio	2-nHex-Ph
1-724	oxathia	2-nHex-Ph
1-725	ozl	2-nHex-Ph
1-726	ozn	2-nHex-Ph
1-727	tzl	2-nHex-Ph
1-728	tzn	2-nHex-Ph
1-729	3-HM-cPent	2-nHex-Ph
1-730	4-HM-dioxo	2-nHex-Ph
1-731	4-HM-dithio	2-nHex-Ph
1-732	4-HM-oxathio	2-nHex-Ph
1-733	3,4-diHM-cPent	2-nHex-Ph
1-734	4,5-diHM-dioxo	2-nHex-Ph
1-735	4,5-diHM-dithio	2-nHex-Ph
1-736	4,5-diHM-oxathio	2-nHex-Ph
1-737	3,4-diHE-cPent	2-nHex-Ph
1-738	4,5-diHE-dioxo	2-nHex-Ph
1-739	4,5-diHE-dithio	2-nHex-Ph
1-740	4,5-diHE-oxathio	2-nHex-Ph
1-741	3-HE-cPent	2-nHex-Ph
1-742	4-HE-dioxo	2-nHex-Ph
1-743	4-HE-dithio	2-nHex-Ph
1-744	4-HE-oxathio	2-nHex-Ph
1-745	3-HP-cPent	2-nHex-Ph
1-746	4-HP-dioxo	2-nHex-Ph
1-747	4-HP-dithio	2-nHex-Ph
1-748	4-HP-oxathio	2-nHex-Ph
1-749	3-HB-cPent	2-nHex-Ph
1-750	4-HB-dioxo	2-nHex-Ph

TABLE 1-continued



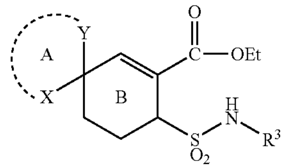
Compound No.	X, Y	R^3
1-751	4-HB-dithio	2-nHex-Ph
1-752	4-HB-oxathio	2-nHex-Ph
1-753	ring 3	2-nHex-Ph
1-754	ring 4	2-nHex-Ph
1-755	ring 5	2-nHex-Ph
1-756	ring 6	2-nHex-Ph
1-757	ring 7	2-nHex-Ph
1-758	ring 8	2-nHex-Ph
1-759	ring 9	2-nHex-Ph
1-760	ring 10	2-nHex-Ph
1-761	3,4-diCH$_2$NHAc-cPent	2-nHex-Ph
1-762	4,5-diCH$_2$NHAc-dioxo	2-nHex-Ph
1-763	4,5-diCH$_2$NHAc-dithio	2-nHex-Ph
1-764	4,5-diCH$_2$NHAc-oxathio	2-nHex-Ph
1-765	ring 11	2-nHex-Ph
1-766	ring 12	2-nHex-Ph
1-767	ring 13	2-nHex-Ph
1-768	ring 14	2-nHex-Ph
1-769	4-OH-cHex	2-nHex-Ph
1-770	5-OH-dioxa	2-nHex-Ph
1-771	5-OH-dithia	2-nHex-Ph
1-772	5-OH-oxathia	2-nHex-Ph
1-773	4-NHAc-cHex	2-nHex-Ph
1-774	5-NHAc-dioxa	2-nHex-Ph
1-775	5-NHAc-dithia	2-nHex-Ph
1-776	5-NHAc-oxathia	2-nHex-Ph
1-777	4,4-diMe-cHex	2-nHex-Ph
1-778	5,5-diMe-dioxa	2-nHex-Ph
1-779	5,5-diMe-dithia	2-nHex-Ph
1-780	5,5-diMe-oxathia	2-nHex-Ph
1-781	4,4-diHM-cHex	2-nHex-Ph
1-782	5,5-diHM-dioxa	2-nHex-Ph
1-783	5,5-diHM-dithia	2-nHex-Ph
1-784	5,5-diHM-oxathia	2-nHex-Ph
1-785	ring 15	2-nHex-Ph
1-786	ring 16	2-nHex-Ph
1-787	ring 17	2-nHex-Ph
1-788	ring 18	2-nHex-Ph
1-789	4,4-diCO$_2$Et-cHex	2-nHex-Ph
1-790	5,5-diCO$_2$Et-dioxa	2-nHex-Ph
1-791	5,5-diCO$_2$Et-dithia	2-nHex-Ph
1-792	5,5-diCO$_2$Et-oxathia	2-nHex-Ph
1-793	O=	4-F-2-nHex-Ph
1-794	S=	4-F-2-nHex-Ph
1-795	cPr	4-F-2-nHex-Ph
1-796	cBu	4-F-2-nHex-Ph
1-797	cPent	4-F-2-nHex-Ph
1-798	cHex	4-F-2-nHex-Ph
1-799	cHept	4-F-2-nHex-Ph
1-800	oxi	4-F-2-nHex-Ph
1-801	oxe	4-F-2-nHex-Ph
1-802	oxo	4-F-2-nHex-Ph
1-803	oxa	4-F-2-nHex-Ph
1-804	dioxo	4-F-2-nHex-Ph
1-805	dioxa	4-F-2-nHex-Ph
1-806	dioxe	4-F-2-nHex-Ph
1-807	dithio	4-F-2-nHex-Ph
1-808	dithia	4-F-2-nHex-Ph
1-809	ring 1	4-F-2-nHex-Ph
1-810	ring 2	4-F-2-nHex-Ph
1-811	oxathio	4-F-2-nHex-Ph
1-812	oxathia	4-F-2-nHex-Ph
1-813	ozl	4-F-2-nHex-Ph
1-814	ozn	4-F-2-nHex-Ph
1-815	tzl	4-F-2-nHex-Ph
1-816	tzn	4-F-2-nHex-Ph
1-817	3-HM-cPent	4-F-2-nHex-Ph
1-818	4-HM-dioxo	4-F-2-nHex-Ph

TABLE 1-continued



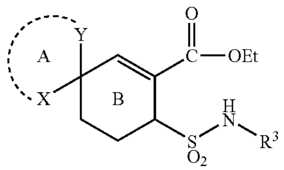
Compound No.	X, Y	R^3
1-819	4-HM-dithio	4-F-2-nHex-Ph
1-820	4-HM-oxathio	4-F-2-nHex-Ph
1-821	3,4-diHM-cPent	4-F-2-nHex-Ph
1-822	4,5-diHM-dioxo	4-F-2-nHex-Ph
1-823	4,5-diHM-dithio	4-F-2-nHex-Ph
1-824	4,5-diHM-oxathio	4-F-2-nHex-Ph
1-825	3,4-diHE-cPent	4-F-2-nHex-Ph
1-826	4,5-diHE-dioxo	4-F-2-nHex-Ph
1-827	4,5-diHE-dithio	4-F-2-nHex-Ph
1-828	4,5-diHE-oxathio	4-F-2-nHex-Ph
1-829	3-HE-cPent	4-F-2-nHex-Ph
1-830	4-HE-dioxo	4-F-2-nHex-Ph
1-831	4-HE-dithio	4-F-2-nHex-Ph
1-832	4-HE-oxathio	4-F-2-nHex-Ph
1-833	3-HP-cPent	4-F-2-nHex-Ph
1-834	4-HP-dioxo	4-F-2-nHex-Ph
1-835	4-HP-dithio	4-F-2-nHex-Ph
1-836	4-HP-oxathio	4-F-2-nHex-Ph
1-837	3-HB-cPent	4-F-2-nHex-Ph
1-838	4-HB-dioxo	4-F-2-nHex-Ph
1-839	4-HB-dithio	4-F-2-nHex-Ph
1-840	4-HB-oxathio	4-F-2-nHex-Ph
1-841	ring 3	4-F-2-nHex-Ph
1-842	ring 4	4-F-2-nHex-Ph
1-843	ring 5	4-F-2-nHex-Ph
1-844	ring 6	4-F-2-nHex-Ph
1-845	ring 7	4-F-2-nHex-Ph
1-846	ring 8	4-F-2-nHex-Ph
1-847	ring 9	4-F-2-nHex-Ph
1-848	ring 10	4-F-2-nHex-Ph
1-849	3,4-diCH$_2$NHAc-cPent	4-F-2-nHex-Ph
1-850	4,5-diCH$_2$NHAc-dioxo	4-F-2-nHex-Ph
1-851	4,5-diCH$_2$NHAc-dithio	4-F-2-nHex-Ph
1-852	4,5-diCH$_2$NHAc-oxathio	4-F-2-nHex-Ph
1-853	ring 11	4-F-2-nHex-Ph
1-854	ring 12	4-F-2-nHex-Ph
1-855	ring 13	4-F-2-nHex-Ph
1-856	ring 14	4-F-2-nHex-Ph
1-857	4-OH-cHex	4-F-2-nHex-Ph
1-858	5-OH-dioxa	4-F-2-nHex-Ph
1-859	5-OH-dithia	4-F-2-nHex-Ph
1-860	5-OH-oxathia	4-F-2-nHex-Ph
1-851	4-NHAc-cHex	4-F-2-nHex-Ph
1-852	5-NHAc-dioxa	4-F-2-nHex-Ph
1-863	5-NHAc-dithia	4-F-2-nHex-Ph
1-854	5-NHAc-oxathia	4-F-2-nHex-Ph
1-865	4,4-diMe-cHex	4-F-2-nHex-Ph
1-866	5,5-diMe-dioxa	4-F-2-nHex-Ph
1-857	5,5-diMe-dithia	4-F-2-nHex-Ph
1-868	5,5-diMe-oxathia	4-F-2-nHex-Ph
1-869	4,4-diHM-cHex	4-F-2-nHex-Ph
1-870	5,5-diHM-dioxa	4-F-2-nHex-Ph
1-871	5,5-diHM-dithia	4-F-2-nHex-Ph
1-872	5,5-diHM-oxathia	4-F-2-nHex-Ph
1-873	ring 15	4-F-2-nHex-Ph
1-874	ring 16	4-F-2-nHex-Ph
1-875	ring 17	4-F-2-nHex-Ph
1-876	ring 18	4-F-2-nHex-Ph
1-877	4,4-diCO$_2$Et-cHex	4-F-2-nHex-Ph
1-878	5,5-diCO$_2$Et-dioxa	4-F-2-nHex-Ph
1-879	5,5-diCO$_2$Et-dithia	4-F-2-nHex-Ph
1-880	5,5-diCO$_2$Et-oxathia	4-F-2-nHex-Ph
1-881	O=	2-nHept-Ph
1-882	S=	2-nHept-Ph
1-883	cPr	2-nHept-Ph
1-884	cBu	2-nHept-Ph
1-885	cPent	2-nHept-Ph
1-886	cHex	2-nHept-Ph

TABLE 1-continued



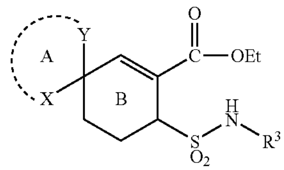
Compound No.	X, Y	R^3
1-887	cHept	2-nHept-Ph
1-888	oxi	2-nHept-Ph
1-889	oxe	2-nHept-Ph
1-890	oxo	2-nHept-Ph
1-891	oxa	2-nHept-Ph
1-892	dioxo	2-nHept-Ph
1-893	dioxa	2-nHept-Ph
1-894	dioxe	2-nHept-Ph
1-895	dithio	2-nHept-Ph
1-896	dithia	2-nHept-Ph
1-897	ring 1	2-nHept-Ph
1-898	ring 2	2-nHept-Ph
1-899	oxathio	2-nHept-Ph
1-900	oxathia	2-nHept-Ph
1-901	ozl	2-nHept-Ph
1-902	ozn	2-nHept-Ph
1-903	tzl	2-nHept-Ph
1-904	tzn	2-nHept-Ph
1-905	3-HM-cPent	2-nHept-Ph
1-906	4-HM-dioxo	2-nHept-Ph
1-907	4-HM-dithio	2-nHept-Ph
1-908	4-HM-oxathio	2-nHept-Ph
1-909	3,4-diHM-cPent	2-nHept-Ph
1-910	4,5-diHM-dioxo	2-nHept-Ph
1-911	4,5-diHM-dithio	2-nHept-Ph
1-912	4,5-diHM-oxathio	2-nHept-Ph
1-913	3,4-diHE-cPent	2-nHept-Ph
1-914	4,5-diHE-dioxo	2-nHept-Ph
1-915	4,5-diHE-dithio	2-nHept-Ph
1-916	4,5-diHE-oxathio	2-nHept-Ph
1-917	3-HE-cPent	2-nHept-Ph
1-918	4-HE-dioxo	2-nHept-Ph
1-919	4-HE-dithio	2-nHept-Ph
1-920	4-HE-oxathio	2-nHept-Ph
1-921	3-HP-cPent	2-nHept-Ph
1-922	4-HP-dioxo	2-nHept-Ph
1-923	4-HP-dithio	2-nHept-Ph
1-924	4-HP-oxathio	2-nHept-Ph
1-925	3-HB-oPent	2-nHept-Ph
1-926	4-HB-dioxo	2-nHept-Ph
1-927	4-HB-dithio	2-nHept-Ph
1-928	4-HB-oxathio	2-nHept-Ph
1-929	ring 3	2-nHept-Ph
1-930	ring 4	2-nHept-Ph
1-931	ring 5	2-nHept-Ph
1-932	ring 6	2-nHept-Ph
1-933	ring 7	2-nHept-Ph
1-934	ring 8	2-nHept-Ph
1-935	ring 9	2-nHept-Ph
1-936	ring 10	2-nHept-Ph
1-937	3,4-diCH$_2$NHAc-cPent	2-nHept-Ph
1-938	4,5-diCH$_2$NHAc-dioxo	2-nHept-Ph
1-939	4,5-diCH$_2$NHAc-dithio	2-nHept-Ph
1-940	4,5-diCH$_2$NHAc-oxathi	2-nHept-Ph
1-941	ring 11	2-nHept-Ph
1-942	ring 12	2-nHept-Ph
1-943	ring 13	2-nHept-Ph
1-944	ring 14	2-nHept-Ph
1-945	4-OH-cHex	2-nHept-Ph
1-946	5-OH-dioxa	2-nHept-Ph
1-947	5-OH-dithia	2-nHept-Ph
1-948	5-OH-oxathia	2-nHept-Ph
1-949	4-NHAc-cHex	2-nHept-Ph
1-950	5-NHAc-dioxa	2-nHept-Ph
1-951	5-NHAc-dithia	2-nHept-Ph
1-952	5-NHAc-oxathia	2-nHept-Ph
1-953	4,4-diMe-cHex	2-nHept-Ph
1-954	5,5-diMe-dioxa	2-nHept-Ph

TABLE 1-continued



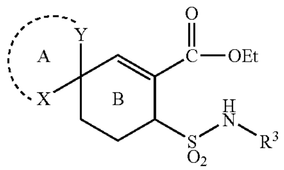
Compound No.	X, Y	R^3
1-955	5,5-diMe-dithia	2-nHept-Ph
1-956	5,5-diMe-oxathia	2-nHept-Ph
1-957	4,4-diHM-cHex	2-nHept-Ph
1-958	5,5-diHM-dioxa	2-nHept-Ph
1-959	5,5-diHM-dithia	2-nHept-Ph
1-960	5,5-diHM-oxathia	2-nHept-Ph
1-961	ring 15	2-nHept-Ph
1-962	ring 16	2-nHept-Ph
1-963	ring 17	2-nHept-Ph
1-964	ring 18	2-nHept-Ph
1-965	4,4-diCO_2Et-cHex	2-nHept-Ph
1-966	5,5-diCO_2Et-dioxa	2-nHept-Ph
1-967	5,5-diCO_2Et-dithia	2-nHept-Ph
1-968	5,5-diCO_2Et-oxathia	2-nHept-Ph
1-969	O=	4-F-2-nHept-Ph
1-970	S=	4-F-2-nHept-Ph
1-971	cPr	4-F-2-nHept-Ph
1-972	cBu	4-F-2-nHept-Ph
1-973	cPent	4-F-2-nHept-Ph
1-974	cHex	4-F-2-nHept-Ph
1-975	cHept	4-F-2-nHept-Ph
1-976	oxi	4-F-2-nHept-Ph
1-977	oxe	4-F-2-nHept-Ph
1-978	oxo	4-F-2-nHept-Ph
1-979	oxa	4-F-2-nHept-Ph
1-980	dioxo	4-F-2-nHept-Ph
1-981	dioxa	4-F-2-nHept-Ph
1-982	dioxe	4-F-2-nHept-Ph
1-983	dithio	4-F-2-nHept-Ph
1-984	dithia	4-F-2-nHept-Ph
1-985	ring 1	4-F-2-nHept-Ph
1-986	ring 2	4-F-2-nHept-Ph
1-987	oxathio	4-F-2-nHept-Ph
1-988	oxathia	4-F-2-nHept-Ph
1-989	ozl	4-F-2-nHept-Ph
1-990	ozn	4-F-2-nHept-Ph
1-991	tzl	4-F-2-nHept-Ph
1-992	tzn	4-F-2-nHept-Ph
1-993	3-HM-cPent	4-F-2-nHept-Ph
1-994	4-HM-dioxo	4-F-2-nHept-Ph
1-995	4-HM-dithio	4-F-2-nHept-Ph
1-996	4-HM-oxathio	4-F-2-nHept-Ph
1-997	3,4-diHM-cPent	4-F-2-nHept-Ph
1-998	4,5-diHM-dioxo	4-F-2-nHept-Ph
1-999	4,5-diHM-dithio	4-F-2-nHept-Ph
1-1000	4,5-diHM-oxathio	4-F-2-nHept-Ph
1-1001	3,4-diHE-cPent	4-F-2-nHept-Ph
1-1002	4,5-diHE-dioxo	4-F-2-nHept-Ph
1-1003	4,5-diHE-dithio	4-F-2-nHept-Ph
1-1004	4,5-diHE-oxathio	4-F-2-nHept-Ph
1-1005	3-HE-cPent	4-F-2-nHept-Ph
1-1006	4-HE-dioxo	4-F-2-nHept-Ph
1-1007	4-HE-dithio	4-F-2-nHept-Ph
1-1008	4-HE-oxathio	4-F-2-nHept-Ph
1-1009	3-HP-cPent	4-F-2-nHept-Ph
1-1010	4-HP-dioxo	4-F-2-nHept-Ph
1-1011	4-HP-dithio	4-F-2-nHept-Ph
1-1012	4-HP-oxathio	4-F-2-nHept-Ph
1-1013	3-HB-cPent	4-F-2-nHept-Ph
1-1014	4-HB-dioxo	4-F-2-nHept-Ph
1-1015	4-HB-dithio	4-F-2-nHept-Ph
1-1016	4-HB-oxathio	4-F-2-nHept-Ph
1-1017	ring 3	4-F-2-nHept-Ph
1-1018	ring 4	4-F-2-nHept-Ph
1-1019	ring 5	4-F-2-nHept-Ph
1-1020	ring 6	4-F-2-nHept-Ph
1-1021	ring 7	4-F-2-nHept-Ph
1-1022	ring 8	4-F-2-nHept-Ph

TABLE 1-continued



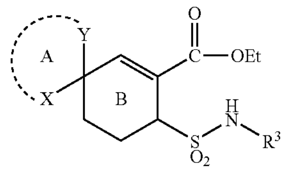
Compound No.	X, Y	R^3
1-1023	ring 9	4-P-2-nHept-Ph
1-1024	ring 10	4-F-2-nHept-Ph
1-1025	3,4-diCH_2NHAc-cPent	4-F-2-nHept-Ph
1-1026	4,5-diCH_2NHAc-dioxo	4-F-2-nHept-Ph
1-1027	4,5-diCH_2NHAc-dithio	4-F-2-nHept-Ph
1-1028	4,5-diCH_2NHAc-oxathio	4-F-2-nHept-Ph
1-1029	ring 11	4-F-2-nHept-Ph
1-1030	ring 12	4-F-2-nHept-Ph
1-1031	ring 13	4-F-2-nHept-Ph
1-1032	ring 14	4-F-2-nHept-Ph
1-1033	4-OH-cHex	4-F-2-nHept-Ph
1-1034	5-OH-dioxa	4-F-2-nHept-Ph
1-1035	5-OH-dithia	4-F-2-nHept-Ph
1-1036	5-OH-oxathia	4-F-2-nHept-Ph
1-1037	4-NHAc-cHex	4-F-2-nHept-Ph
1-1038	5-NHAc-dioxa	4-F-2-nHept-Ph
1-1039	5-NHAc-dithia	4-F-2-nHept-Ph
1-1040	5-NHAc-oxathia	4-F-2-nHept-Ph
1-1041	4,4-diMe-cHex	4-F-2-nHept-Ph
1-1042	5,5-diMe-dioxa	4-F-2-nHept-Ph
1-1043	5,5-diMe-dithia	4-F-2-nHept-Ph
1-1044	5,5-diMe-oxathia	4-F-2-nHept-Ph
1-1045	4,4-diHM-cHex	4-F-2-nHept-Ph
1-1046	5,5-diHM-dioxa	4-F-2-nHept-Ph
1-1047	5, 5-diHM-dithia	4-F-2-nHept-Ph
1-1048	5, 5-diHM-oxathia	4-F-2-nHept-Ph
1-1049	ring 15	4-F-2-nHept-Ph
1-1050	ring 16	4-F-2-nHept-Ph
1-1051	ring 17	4-F-2-nHept-Ph
1-1052	ring 18	4-F-2-nHept-Ph
1-1053	4,4-diCO_2Et-cHex	4-F-2-nHept-Ph
1-1054	5,5-diCO_2Et-dioxa	4-F-2-nHept-Ph
1-1055	5,5-diCO_2Et-dithia	4-F-2-nHept-Ph
1-1056	5,5-diCO_2Et-oxathia	4-F-2-nHept-Ph
1-1057	H,H	Pyr
1-1058	O=	Pyr
1-1059	S=	Pyr
1-1060	cPent	Pyr
1-1061	cHex	Pyr
1-1062	dioxo	Pyr
1-1063	dioxa	Pyr
1-1064	dithio	Pyr
1-1065	dithia	Pyr
1-1066	oxathio	Pyr
1-1067	oxathia	Pyr
1-1068	4-HM-dioxo	Pyr
1-1069	4,5-diHM-dioxo	Pyr
1-1070	4,5-diHE-dioxo	Pyr
1-1071	5-OH-dioxa	Pyr
1-1072	5-NHAc-dioxa	Pyr
1-1073	5,5-diHM-dioxa	Pyr
1-1074	H,H	2-F-Pyr
1-1075	O=	2-F-Pyr
1-1076	S=	2-F-Pyr
1-1077	cPent	2-F-Pyr
1-1078	cHex	2-F-Pyr
1-1079	dioxo	2-F-Pyr
1-1080	dioxa	2-F-Pyr
1-1081	dithio	2-F-Pyr
1-1082	dithia	2-F-Pyr
1-1083	oxathia	2-F-Pyr
1-1084	oxathia	2-F-Pyr
1-1085	4-HM-dioxo	2-F-Pyr
1-1086	4,5-diHM-dioxo	2-F-Pyr
1-1087	4,5-diHE-dioxo	2-F-Pyr
1-1088	5-OH-dioxa	2-F-Pyr
1-1089	5-NHAc-dioxa	2-F-Pyr
1-1090	5,5-diHM-dioxa	2-F-Pyr

TABLE 1-continued



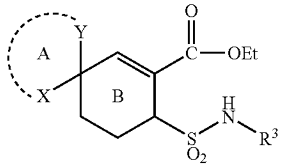
Compound No.	X, Y	R^3
1-1091	H,H	2-Cl-Pyr
1-1092	O═	2-Cl-Pyr
1-1093	S═	2-Cl-Pyr
1-1094	cPent	2-Cl-Pyr
1-1095	cHex	2-Cl-Pyr
1-1096	dioxo	2-Cl-Pyr
1-1097	dioxa	2-Cl-Pyr
1-1098	dithio	2-Cl-Pyr
1-1099	dithia	2-Cl-Pyr
1-1100	oxathio	2-Cl-Pyr
1-1101	oxathia	2-Cl-Pyr
1-1102	4-HM-dioxo	2-Cl-Pyr
1-1103	4,5-diHM-dioxo	2-Cl-Pyr
1-1104	4,5-diHE-dioxo	2-Cl-Fyr
1-1105	5-OH-dioxa	2-Cl-Pyr
1-1106	5-NHAc-dioxa	2-Cl-Pyr
1-1107	5,5-diHM-dioxa	2-Cl-Pyr
1-1108	H,H	2-Br-Pyr
1-1109	O═	2-Br-Pyr
1-1110	S═	2-Br-Pyr
1-1111	cPent	2-Br-Pyr
1-1112	cHex	2-Br-Pyr
1-1113	dioxo	2-Br-Pyr
1-1114	dioxa	2-Br-Pyr
1-1115	dithio	2-Br-Pyr
1-1116	dithia	2-Br-Pyr
1-1117	oxathio	2-Br-Pyr
1-1118	oxathia	2-Br-Pyr
1-1119	4-HM-dioxo	2-Br-Pyr
1-1120	4,5-diHM-dioxo	2-Br-Pyr
1-1121	4,5-diHE-dioxo	2-Br-Pyr
1-1122	5-OH-dioxa	2-Br-Pyr
1-1123	5-NHAc-dioxa	2-Br-Pyr
1-1124	5,5-diHM-dioxa	2-Br-Pyr
1-1125	H,H	2,5-diF-Pyr
1-1126	O═	2,5-diF-Pyr
1-1127	S═	2,5-diF-Pyr
1-1128	cPent	2,5-diF-Pyr
1-1129	cHex	2,5-diF-Pyr
1-1130	dioxo	2,5-diF-Pyr
1-1131	dioxa	2,5-diF-Pyr
1-1132	dithio	2,5-diF-Pyr
1-1133	dithia	2,5-diF-Pyr
1-1134	oxathio	2,5-diF-Pyr
1-1135	oxathia	2,5-diF-Pyr
1-1136	4-HM-dioxo	2,5-diF-Pyr
1-1137	4,5-diHM-dioxo	2,5-diF-Pyr
1-1138	4,5-diHE-dioxo	2,5-diF-Pyr
1-1139	5-OH-dioxa	2,5-diF-Pyr
1-1140	5-NHAc-dioxa	2,5-diF-Pyr
1-1141	5,5-diHM-dioxa	2,5-diF-Pyr
1-1142	H,H	2 5-diCl-Pyr
1-1143	O═	2,5-diCl-Pyr
1-1144	S═	2,5-diCl-Pyr
1-1145	cPent	2,5-diCl-Pyr
1-1146	cHex	2,5-diCl-Pyr
1-1147	dioxo	2,5-diCl-Pyr
1-1148	dioxa	2,5-diCl-Pyr
1-1149	dithio	2,5-diCl-Pyr
1-1150	dithia	2,5-diCl-Pyr
1-1151	oxathio	2,5-diCl-Pyr
1-1152	oxathia	2,5-diCl-Pyr
1-1153	4-HM-dioxo	2,5-diCl-Pyr
1-1154	4,5-diHM-dioxo	2,5-diCl-Pyr
1-1155	4,5-diHE-dioxo	2,5-diCl-Pyr
1-1156	5-OH-dioxa	2,5-diCl-Pyr
1-1157	5-NHAc-dioxa	2,5-diCl-Pyr
1-1158	5,5-diHM-dioxa	2,5-diCl-Pyr

TABLE 1-continued



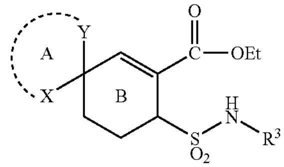
Compound No.	X, Y	R^3
1-1159	H,H	2,5-diBr-Pyr
1-1160	O═	2,5-diBr-Pyr
1-1161	S═	2,5-diBr-Pyr
1-1162	cPent	2,5-diBr-Pyr
1-1163	cHex	2,5-diBr-Pyr
1-1164	dioxo	2,5-diBr-Pyr
1-1165	dioxa	2,5-diBr-Pyr
1-1166	dithio	2,5-diBr-Pyr
1-1167	dithia	2,5-diBr-Pyr
1-1168	oxathio	2,5-diBr-Pyr
1-1169	oxathia	2,5-diBr-Pyr
1-1170	4-HM-dioxo	2,5-diBr-Pyr
1-1171	4,5-diHM-dioxo	2,5-diBr-Pyr
1-1172	4,5-diHE-dioxo	2,5-diBr-Pyr
1-1173	5-OH-dioxa	2,5-diBr-Pyr
1-1174	5-NHAc-dioxa	2,5-diBr-Pyr
1-1175	5,5-diHM-dioxa	2,5-diBr-Pyr
1-1176	H,H	2-Me-Pyr
1-1177	O═	2-Me-Pyr
1-1178	S═	2-Me-Pyr
1-1179	cPent	2-Me-Pyr
1-1180	cHex	2-Me-Pyr
1-1181	dioxo	2-Me-Pyr
1-1182	dioxa	2-Me-Pyr
1-1183	dithio	2-Me-Pyr
1-1184	dithia	2-Me-Pyr
1-1185	oxathio	2-Me-Pyr
1-1186	oxathia	2-Me-Pyr
1-1187	4-HM-dioxo	2-Me-Pyr
1-1188	4,5-diHM-dioxo	2-Me-Pyr
1-1189	4,5-diHE-dioxo	2-Me-Pyr
1-1190	5-OH-dioxa	2-Me-Pyr
1-1191	5-NHAc-dioxa	2-Me-Pyr
1-1192	5,5-diHM-dioxa	2-Me-Pyr
1-1193	H,H	2-Et-Pyr
1-1194	O═	2-Et-Pyr
1-1195	S═	2-Et-Pyr
1-1196	cPent	2-Et-Pyr
1-1197	cHex	2-Et-Pyr
1-1198	dioxo	2-Et-Pyr
1-1199	dioxa	2-Et-Pyr
1-1200	dithio	2-Et-Pyr
1-1201	dithia	2-Et-Pyr
1-1202	oxathio	2-Et-Pyr
1-1203	oxathia	2-Et-Pyr
1-1204	4-HM-dioxo	2-Et-Pyr
1-1205	4,5-diHM-dioxo	2-Et-Pyr
1-1206	4,5-diHE-dioxo	2-Et-Pyr
1-1207	5-OH-dioxa	2-Et-Pyr
1-1208	5-NHAc-dioxa	2-Et-Pyr
1-1209	5,5-diHM-dioxa	2-Et-Pyr
1-1210	H,H	2-nPr-Pyr
1-1211	O═	2-nPr-Pyr
1-1212	S═	2-nPr-Pyr
1-1213	cPent	2-nPr-Pyr
1-1214	cHex	2-nPr-Pyr
1-1215	dioxo	2-nPr-Pyr
1-1216	dioxa	2-nPr-Pyr
1-1217	dithio	2-nPr-Pyr
1-1218	dithia	2-nPr-Pyr
1-1219	oxathio	2-nPr-Pyr
1-1220	oxathia	2-nPr-Pyr
1-1221	4-HM-dioxo	2-nPr-Pyr
1-1222	4,5-diHM-dioxo	2-nPr-Pyr
1-1223	4,5-diHE-dioxo	2-nPr-Pyr
1-1224	5-OH-dioxa	2-nPr-Pyr
1-1225	5-NHAc-dioxa	2-nPr-Pyr
1-1226	5,5-diHM-dioxa	2-nPr-Pyr

TABLE 1-continued



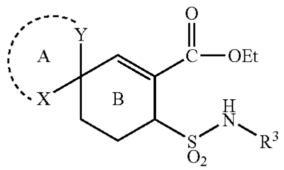
Compound No.	X, Y	R^3
1-1227	H,H	2-nBu-Pyr
1-1228	O═	2-nBu-Pyr
1-1229	S═	2-nBu-Pyr
1-1230	cPent	2-nBu-Pyr
1-1231	cHex	2-nBu-Pyr
1-1232	dioxo	2-nBu-Pyr
1-1233	dioxa	2-nBu-Pyr
1-1234	dithio	2-nBu-Pyr
1-1235	dithia	2-nBu-Pyr
1-1236	oxathio	2-nBu-Pyr
1-1237	oxathia	2-nBu-Pyr
1-1238	4-HM-dioxo	2-nBu-Pyr
1-1239	4,5-diHM-dioxo	2-nBu-Pyr
1-1240	4,5-diHE-dioxo	2-nBu-Pyr
1-1241	5-OH-dioxa	2-nBu-Pyr
1-1242	5-NHAc-dioxa	2-nBu-Pyr
1-1243	5,5-diHM-dioxa	2-nBu-Pyr
1-1244	H,H	2-nPent-Pyr
1-1245	O═	2-nPent-Pyr
1-1246	S═	2-nPent-Pyr
1-1247	cPent	2-nPent-Pyr
1-1248	cHex	2-nPent-Pyr
1-1249	dioxo	2-nPent-Pyr
1-1250	dioxa	2-nPent-Pyr
1-1251	dithio	2-nPent-Pyr
1-1252	dithia	2-nPent-Pyr
1-1253	oxathio	2-nPent-Pyr
1-1254	oxathia	2-nPent-Pyr
1-1255	4-HM-dioxo	2-nPent-Pyr
1-1256	4,5-diHM-dioxo	2-nPent-Pyr
1-1257	4,5-diHE-dioxo	2-nPent-Pyr
1-1258	5-OH-dioxa	2-nPent-Pyr
1-1259	5-NHAc-dioxa	2-nPent-Pyr
1-1260	5,5-diHM-dioxa	2-nPent-Pyr
1-1261	H,H	2-nHex-Pyr
1-1262	O═	2-nHex-Pyr
1-1263	S═	2-nHex-Pyr
1-1264	cPent	2-nHex-Pyr
1-1265	cHex	2-nHex-Pyr
1-1266	dioxo	2-nHex-Pyr
1-1267	dioxa	2-nHex-Pyr
1-1268	dithio	2-nHex-Pyr
1-1269	dithia	2-nHex-Pyr
1-1270	oxathio	2-nHex-Pyr
1-1271	oxathia	2-nHex-Pyr
1-1272	4-HM-dioxo	2-nHex-Pyr
1-1273	4,5-diHM-dioxo	2-nHex-Pyr
1-1274	4,5-diHE-dioxo	2-nHex-Pyr
1-1275	5-OH-dioxa	2-nHex-Pyr
1-1276	5-NHAc-dioxa	2-nHex-Pyr
1-1277	5,5-diHM-dioxa	2-nHex-Pyr
1-1278	H,H	2-nHept-Pyr
1-1279	O═	2-nHept-Pyr
1-1280	S═	2-nHept-Pyr
1-1281	cPent	2-nHept-Pyr
1-1282	cHex	2-nHept-Pyr
1-1283	dioxo	2-nHept-Pyr
1-1284	dioxa	2-nHept-Pyr
1-1285	dithio	2-nHept-Pyr
1-1286	dithia	2-nHept-Pyr
1-1287	oxathio	2-nHept-Pyr
1-1288	oxathia	2-nHept-Pyr
1-1289	4-HM-dioxo	2-nHept-Pyr
1-1290	4,5-diHM-dioxo	2-nHept-Pyr
1-1291	4,5-diHE-dioxo	2-nHept-Pyr
1-1292	5-OH-dioxa	2-nHept-Pyr
1-1293	5-NHAc-dioxa	2-nHept-Pyr
1-1294	5,5-diHM-dioxa	2-nHept-Pyr

TABLE 1-continued



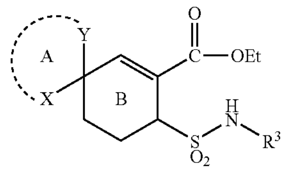
Compound No.	X, Y	R^3
1-1295	H,H	2-nOct-Pyr
1-1296	O═	2-nOct-Pyr
1-1297	S═	2-nOct-Pyr
1-1298	cPent	2-nOct-Pyr
1-1299	cHex	2-nOct-Pyr
1-1300	dioxo	2-nOct-Pyr
1-1301	dioxa	2-nOct-Pyr
1-1302	dithio	2-nOct-Pyr
1-1303	dithia	2-nOct-Pyr
1-1304	oxathio	2-nOct-Pyr
1-1305	oxathia	2-nOct-Pyr
1-1306	4-HM-dioxo	2-nOct-Pyr
1-1307	4,5-diHM-dioxo	2-nOct-Pyr
1-1308	4,5-diHE-dioxo	2-nOct-Pyr
1-1309	5-OH-dioxa	2-nOct-Pyr
1-1310	5-NHAc-dioxa	2-nOct-Pyr
1-1311	5,5-diHM-dioxa	2-nOct-Pyr
1-1312	H,H	2-cPrl-Pyr
1-1313	O═	2-cPrl-Pyr
1-1314	S═	2-cPrl-Pyr
1-1315	cPent	2-cPrl-Pyr
1-1316	cHex	2-cPrl-Pyr
1-1317	dioxo	2-cPrl-Pyr
1-1318	dioxa	2-cPrl-Pyr
1-1319	dithio	2-cPrl-Pyr
1-1320	dithia	2-cPrl-Pyr
1-1321	oxathio	2-cPrl-Pyr
1-1322	oxathia	2-cPrl-Pyr
1-1323	4-HM-dioxo	2-cPrl-Pyr
1-1324	4,5-diHM-dioxo	2-cPrl-Pyr
1-1325	4,5-diHE-dioxo	2-cPrl-Pyr
1-1326	5-OH-dioxa	2-cPrl-Pyr
1-1327	5-NHAc-dioxa	2-cPrl-Pyr
1-1328	5,5-diHM-dioxa	2-cPrl-Pyr
1-1329	H,H	2-Ph-Pyr
1-1330	O═	2-Ph-Pyr
1-1331	S═	2-Ph-Pyr
1-1332	cPent	2-Ph-Pyr
1-1333	cHex	2-Ph-Pyr
1-1334	dioxo	2-Ph-Pyr
1-1335	dioxa	2-Ph-Pyr
1-1336	dithio	2-Ph-Pyr
1-1337	dithia	2-Ph-Pyr
1-1338	oxathio	2-Ph-Pyr
1-1339	oxathia	2-Ph-Pyr
1-1340	4-HM-dioxo	2-Ph-Pyr
1-1341	4,5-diHM-dioxo	2-Ph-Pyr
1-1342	4,5-diHE-dioxo	2-Ph-Pyr
1-1343	5-OH-dioxa	2-Ph-Pyr
1-1344	5-NHAc-dioxa	2-Ph-Pyr
1-1345	5,5-diHM-dioxa	2-Ph-Pyr
1-1346	H,H	2,5-diMe-Pyr
1-1347	O═	2,5-diMe-Pyr
1-1348	S═	2,5-diMe-Pyr
1-1349	cPent	2,5-diMe-Pyr
1-1350	cHex	2,5-diMe-Pyr
1-1351	dioxo	2,5-diMe-Pyr
1-1352	dioxa	2,5-diMe-Pyr
1-1353	dithio	2,5-diMe-Pyr
1-1354	dithia	2,5-diMe-Pyr
1-1355	oxathio	2,5-diMe-Pyr
1-1356	oxathia	2,5-diMe-Pyr
1-1357	4-HM-dioxo	2,5-diMe-Pyr
1-1358	4,5-diHM-dioxo	2,5-diMe-Pyr
1-1359	4,5-diHE-dioxo	2,5-diMe-Pyr
1-1360	5-OH-dioxa	2,5-diMe-Pyr
1-1361	5-NHAc-dioxa	2,5-diMe-Pyr
1-1362	5,5-diHM-dioxa	2,5-diMe-Pyr

TABLE 1-continued



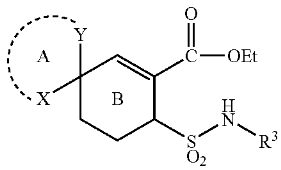
Compound No.	X, Y	R^3
1-1363	O═	2-Br-Ph
1-1364	S═	2-Br-Ph
1-1365	cPr	2-Br-Ph
1-1366	cBu	2-Br-Ph
1-1367	cPent	2-Br-Ph
1-1368	cHex	2-Br-Ph
1-1369	cHept	2-Br-Ph
1-1370	oxi	2-Br-Ph
1-1371	oxe	2-Br-Ph
1-1372	oxo	2-Br-Ph
1-1373	oxa	2-Br-Ph
1-1374	dioxo	2-Br-Ph
1-1375	dioxa	2-Br-Ph
1-1376	dioxe	2-Br-Ph
1-1377	dithio	2-Br-Ph
1-1378	dithia	2-Br-Ph
1-1379	ring 1	2-Br-Ph
1-1380	ring 2	2-Br-Ph
1-1381	oxathio	2-Br-Ph
1-1382	oxathia	2-Br-Ph
1-1383	ozl	2-Br-Ph
1-1384	ozn	2-Br-Ph
1-1385	tzl	2-Br-Ph
1-1386	tzn	2-Br-Ph
1-1387	3-HM-cPent	2-Br-Ph
1-1388	4-HM-dioxo	2-Br-Ph
1-1389	4-HM-dithio	2-Br-Ph
1-1390	4-HM-oxathio	2-Br-Ph
1-1391	3,4-diHM-cPent	2-Br-Ph
1-1392	4,5-diHM-dioxo	2-Br-Ph
1-1393	4,5-diHM-dithio	2-Br-Ph
1-1394	4,5-diHM-oxathio	2-Br-Ph
1-1395	3,4-diHE-cPent	2-Br-Ph
1-1396	4,5-diHE-dioxo	2-Br-Ph
1-1397	4,5-diHE-dithio	2-Br-Ph
1-1398	4,5-diHE-oxathio	2-Br-Ph
1-1399	3-HE-cPent	2-Br-Ph
1-1400	4-HE-dioxo	2-Br-Ph
1-1401	4-HE-dithio	2-Br-Ph
1-1402	4-HE-oxathio	2-Br-Ph
1-1403	3-HP-cPent	2-Br-Ph
1-1404	4-HP-dioxo	2-Br-Ph
1-1405	4-HP-dithio	2-Br-Ph
1-1406	4-HP-oxathio	2-Br-Ph
1-1407	3-HB-cPent	2-Br-Ph
1-1408	4-HB-dioxo	2-Br-Ph
1-1409	4-HB-dithio	2-Br-Ph
1-1410	4-HB-oxathio	2-Br-Ph
1-1411	ring 3	2-Br-Ph
1-1412	ring 4	2-Br-Ph
1-1413	ring 5	2-Br-Ph
1-1414	ring 6	2-Br-Ph
1-1415	ring 7	2-Br-Ph
1-1416	ring 8	2-Br-Ph
1-1417	ring 9	2-Br-Ph
1-1418	ring 10	2-Br-Ph
1-1419	3,4-diCH_2NHAc-cPent	2-Br-Ph
1-1420	4,5-diCH_2NHAc-dioxo	2-Br-Ph
1-1421	4,5-diCH_2NHAc-dithio	2-Br-Ph
1-1422	4,5-diCH_2NHAc-oxathio	2-Br-Ph
1-1423	ring 11	2-Br-Ph
1-1424	ring 12	2-Br-Ph
1-1425	ring 13	2-Br-Ph
1-1426	ring 14	2-Br-Ph
1-1427	4-OH-cHex	2-Br-Ph
1-1428	5-OH-dioxa	2-Br-Ph
1-1429	5-OH-dithia	2-Br-Ph
1-1430	5-OH-oxathia	2-Br-Ph

TABLE 1-continued



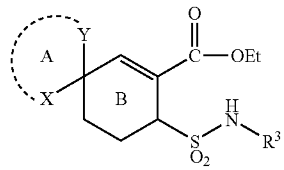
Compound No.	X, Y	R^3
1-1431	4-NHAc-cHex	2-Br-Ph
1-1432	5-NHAc-dioxa	2-Br-Ph
1-1433	5-NHAc-dithia	2-Br-Ph
1-1434	5-NHAc-oxathia	2-Br-Ph
1-1435	4,4-diMe-cHex	2-Br-Ph
1-1436	5,5-diMe-dioxa	2-Br-Ph
1-1437	5,5-diMe-dithia	2-Br-Ph
1-1438	5,5-diMe-oxathia	2-Br-Ph
1-1439	4,4-diHM-cHex	2-Br-Ph
1-1440	5,5-diHM-dioxa	2-Br-Ph
1-1441	5,5-diHM-dithia	2-Br-Ph
1-1442	5,5-diHM-oxathia	2-Br-Ph
1-1443	ring 15	2-Br-Ph
1-1444	ring 16	2-Br-Ph
1-1445	ring 17	2-Br-Ph
1-1446	ring 18	2-Br-Ph
1-1447	4,4-diCO_2Et-cHex	2-Br-Ph
1-1448	5,5-diCO_2Et-dioxa	2-Br-Ph
1-1449	5,5-diCO_2Et-dithia	2-Br-Ph
1-1450	5,5-diCO_2Et-oxathia	2-Br-Ph
1-1451	O═	2-Cl-6-Me-Ph
1-1452	S═	2-Cl-6-Me-Ph
1-1453	cPr	2-Cl-6-Me-Ph
1-1454	cBu	2-Cl-6-Me-Ph
1-1455	cPent	2-Cl-6-Me-Ph
1-1456	cHex	2-Cl-6-Me-Ph
1-1457	cHept	2-Cl-6-Me-Ph
1-1458	oxi	2-Cl-6-Me-Ph
1-1459	oxe	2-Cl-6-Me-Ph
1-1460	oxo	2-Cl-6-Me-Ph
1-1461	oxa	2-Cl-6-Me-Ph
1-1462	dioxo	2-Cl-6-Me-Ph
1-1463	dioxa	2-Cl-6-Me-Ph
1-1464	dioxe	2-Cl-6-Me-Ph
1-1465	dithio	2-Cl-6-Me-Ph
1-1466	dithia	2-Cl-6-Me-Ph
1-1467	ring 1	2-Cl-6-Me-Ph
1-1468	ring 2	2-Cl-6-Me-Ph
1-1469	oxathio	2-Cl-6-Me-Ph
1-1470	oxathia	2-Cl-6-Me-Ph
1-1471	ozl	2-Cl-6-Me-Ph
1-1472	ozn	2-Cl-6-Me-Ph
1-1473	tzl	2-Cl-6-Me-Ph
1-1474	tzn	2-Cl-6-Me-Ph
1-1475	3-HM-cPent	2-Cl-6-Me-Ph
1-1476	4-HM-dioxo	2-Cl-6-Me-Ph
1-1477	4-HM-dithio	2-Cl-6-Me-Ph
1-1478	4-HM-oxathio	2-Cl-6-Me-Ph
1-1479	3,4-diHM-cPent	2-Cl-6-Me-Ph
1-1480	4,5-diHM-dioxo	2-Cl-6-Me-Ph
1-1481	4,5-diHM-dithio	2-Cl-6-Me-Ph
1-1482	4,5-diHM-oxathio	2-Cl-6-Me-Ph
1-1483	3,4-diHE-cPent	2-Cl-6-Me-Ph
1-1484	4,5-diHE-dioxo	2-Cl-6-Me-Ph
1-1485	4,5-diHE-dithio	2-Cl-6-Me-Ph
1-1486	4,5-diHE-oxathio	2-Cl-6-Me-Ph
1-1487	3-HE-cPent	2-Cl-6-Me-Ph
1-1488	4-HE-dioxo	2-Cl-6-Me-Ph
1-1489	4-HE-dithio	2-Cl-6-Me-Ph
1-1490	4-HE-oxathio	2-Cl-6-Me-Ph
1-1491	3-HP-cPent	2-Cl-6-Me-Ph
1-1492	4-HP-dioxo	2-Cl-6-Me-Ph
1-1493	4-HP-dithio	2-Cl-6-Me-Ph
1-1494	4-HP-oxathio	2-Cl-6-Me-Ph
1-1495	3-HB-cPent	2-Cl-6-Me-Ph
1-1496	4-HB-dioxo	2-Cl-6-Me-Ph
1-1497	4-HB-dithio	2-Cl-6-Me-Ph
1-1498	4-HB-oxathio	2-Cl-6-Me-Ph

TABLE 1-continued



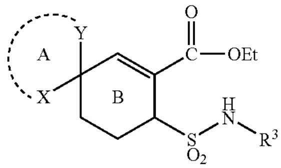
Compound No.	X, Y	R^3
1-1499	ring 3	2-Cl-6-Me-Ph
1-1500	ring 4	2-Cl-6-Me-Ph
1-1501	ring 5	2-Cl-6-Me-Ph
1-1502	ring 6	2-Cl-6-Me-Ph
1-1503	ring 7	2-Cl-6-Me-Ph
1-1504	ring 8	2-Cl-6-Me-Ph
1-1505	ring 9	2-Cl-6-Me-Ph
1-1506	ring 10	2-Cl-6-Me-Ph
1-1507	3,4-diCH_2NHAc-cPent	2-Cl-6-Me-Ph
1-1508	4,5-diCH_2NHAc-dioxo	2-Cl-6-Me-Ph
1-1509	4,5-diCH_2NHAc-dithio	2-Cl-6-Me-Ph
1-1510	4,5-diCH_2NHAc-oxathio	2-Cl-6-Me-Ph
1-1511	ring 11	2-Cl-6-Me-Ph
1-1512	ring 12	2-Cl-6-Me-Ph
1-1513	ring 13	2-Cl-6-Me-Ph
1-1514	ring 14	2-Cl-6-Me-Ph
1-1515	4-OH-cHex	2-Cl-6-Me-Ph
1-1516	5-OH-dioxa	2-Cl-6-Me-Ph
1-1517	5-OH-dithia	2-Cl-6-Me-Ph
1-1518	5-OH-oxathia	2-Cl-6-Me-Ph
1-1519	4-NHAc-cHex	2-Cl-6-Me-Ph
1-1520	5-NHAc-dioxa	2-Cl-6-Me-Ph
1-1521	5-NHAc-dithia	2-Cl-6-Me-Ph
1-1522	5-NHAc-oxathia	2-Cl-6-Me-Ph
1-1523	4,4-diMe-cHex	2-Cl-6-Me-Ph
1-1524	5,5-diMe-dioxa	2-Cl-6-Me-Ph
1-1525	5,5-diMe-dithia	2-Cl-6-Me-Ph
1-1526	5,5-diMe-oxathia	2-Cl-6-Me-Ph
1-1527	4,4-diHM-cHex	2-Cl-6-Me-Ph
1-1528	5,5-diHM-dioxa	2-Cl-6-Me-Ph
1-1529	5,5-diHM-dithia	2-Cl-6-Me-Ph
1-1530	5,5-diHM-oxathia	2-Cl-6-Me-Ph
1-1531	ring 15	2-Cl-6-Me-Ph
1-1532	ring 16	2-Cl-6-Me-Ph
1-1533	ring 17	2-Cl-6-Me-Ph
1-1534	ring 18	2-Cl-6-Me-Ph
1-1535	4,4-diCO_2Et-cHex	2-Cl-6-Me-Ph
1-1536	5,5-diCO_2Et-dioxa	2-Cl-6-Me-Ph
1-1537	5,5-diCO_2Et-dithia	2-Cl-6-Me-Ph
1-1538	5,5-diCO_2Et-oxathia	2-Cl-6-Me-Ph
1-1539	O=	2-Br-4-F-Ph
1-1540	S=	2-Br-4-F-Ph
1-1541	cPr	2-Br-4-F-Ph
1-1542	cBu	2-Br-4-F-Ph
1-1543	cPent	2-Br-4-F-Ph
1-1544	cHex	2-Br-4-F-Ph
1-1545	cHept	2-Br-4-F-Ph
1-1546	oxi	2-Br-4-F-Ph
1-1547	oxe	2-Br-4-F-Ph
1-1548	oxo	2-Br-4-F-Ph
1-1549	oxa	2-Br-4-F-Ph
1-1550	dioxo	2-Br-4-F-Ph
1-1551	dioxa	2-Br-4-F-Ph
1-1552	dioxe	2-Br-4-F-Ph
1-1553	dithio	2-Br-4-F-Ph
1-1554	dithia	2-Br-4-F-Ph
1-1555	ring 1	2-Br-4-F-Ph
1-1556	ring 2	2-Br-4-F-Ph
1-1557	oxathio	2-Br-4-F-Ph
1-1558	oxathia	2-Br-4-F-Ph
1-1559	ozl	2-Br-4-F-Ph
1-1560	ozn	2-Br-4-F-Ph
1-1561	tzl	2-Br-4-F-Ph
1-1562	tzn	2-Br-4-F-Ph
1-1563	3-HM-cPent	2-Br-4-F-Ph
1-1564	4-HM-dioxo	2-Br-4-F-Ph
1-1565	4-HM-dithio	2-Br-4-F-Ph
1-1566	4-HM-oxathio	2-Br-4-F-Ph

TABLE 1-continued



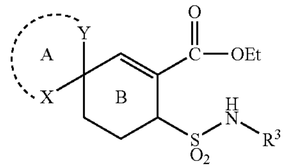
Compound No.	X, Y	R^3
1-1567	3,4-diHM-cPent	2-Br-4-F-Ph
1-1568	4,5-diHM-dioxo	2-Br-4-F-Ph
1-1569	4,5-diHM-dithio	2-Br-4-F-Ph
1-1570	4,5-diHM-oxathio	2-Br-4-P-Ph
1-1571	3,4-diHE-cPent	2-Br-4-F-Ph
1-1572	4,5-diHE-dioxo	2-Br-4-F-Ph
1-1573	4,5-diHE-dithio	2-Br-4-F-Ph
1-1574	4,5-diHE-oxathio	2-Br-4-F-Ph
1-1575	3-HE-cPent	2-Br-4-F-Ph
1-1576	4-HE-dioxo	2-Br-4-F-Ph
1-1577	4-HE-dithio	2-Br-4-F-Ph
1-1578	4-HE-oxathio	2-Br-4-F-Ph
1-1579	3-HP-cPent	2-Br-4-F-Ph
1-1580	4-HP-dioxo	2-Br-4-F-Ph
1-1581	4-HP-dithio	2-Br-4-F-Ph
1-1582	4-HP-oxathio	2-Br-4-F-Ph
1-1583	3-HB-cPent	2-Br-4-F-Ph
1-1584	4-HB-dioxo	2-Br-4-F-Ph
1-1585	4-HB-dithio	2-Br-4-F-Ph
1-1586	4-HB-oxathio	2-Br-4-F-Ph
1-1587	ring 3	2-Br-4-F-Ph
1-1588	ring 4	2-Br-4-F-Ph
1-1589	ring 5	2-Br-4-F-Ph
1-1590	ring 6	2-Br-4-F-Ph
1-1591	ring 7	2-Br-4-F-Ph
1-1592	ring 8	2-Br-4-F-Ph
1-1593	ring 9	2-Br-4-F-Ph
1-1594	ring 10	2-Br-4-F-Ph
1-1595	3,4-diCH_2NHAc-cPent	2-Br-4-F-Ph
1-1596	4,5-diCH_2NHAc-dioxo	2-Br-4-F-Ph
1-1597	4,5-diCH_2NHAc-dithio	2-Br-4-F-Ph
1-1598	4,5-diCH_2NHAc-oxathio	2-Br-4-F-Ph
1-1599	ring 11	2-Br-4-F-Ph
1-1600	ring 12	2-Br-4-F-Ph
1-1601	ring 13	2-Br-4-F-Ph
1-1602	ring 14	2-Br-4-F-Ph
1-1603	4-OH-cHex	2-Br-4-F-Ph
1-1604	5-OH-dioxa	2-Br-4-F-Ph
1-1605	5-OH-dithia	2-Br-4-F-Ph
1-1606	5-OH-oxathia	2-Br-4-F-Ph
1-1607	4-NHAc-cHex	2-Br-4-F-Ph
1-1608	5-NHAc-dioxa	2-Br-4-F-Ph
1-1609	5-NHAc-dithia	2-Br-4-F-Ph
1-1610	5-NHAc-oxathia	2-Br-4-F-Ph
1-1611	4,4-diMe-cHex	2-Br-4-F-Ph
1-1612	5,5-diMe-dioxa	2-Br-4-F-Ph
1-1613	5,5-diMe-dithia	2-Br-4-F-Ph
1-1614	5,5-diMe-oxathia	2-Br-4-F-Ph
1-1615	4,4-diHM-cHex	2-Br-4-F-Ph
1-1616	5,5-diHM-dioxa	2-Br-4-F-Ph
1-1617	5,5-diHM-dithia	2-Br-4-F-Ph
1-1618	5,5-diHM-oxathia	2-Br-4-F-Ph
1-1619	ring 15	2-Br-4-F-Ph
1-1620	ring 16	2-Br-4-F-Ph
1-1621	ring 17	2-Br-4-F-Ph
1-1622	ring 18	2-Br-4-F-Ph
1-1623	4,4-diCO_2Et-cHex	2-Br-4-F-Ph
1-1624	5,5-diCO_2Et-dioxa	2-Br-4-F-Ph
1-1625	5,5-diCO_2Et-dithia	2-Br-4-F-Ph
1-1626	5,5-diCO_2Et-oxathia	2-Br-4-F-Ph
1-1627	O=	2-nPent-Ph
1-1628	S=	2-nPent-Ph
1-1629	cPr	2-nPent-Ph
1-1630	cBu	2-nPent-Ph
1-1631	cPent	2-nPent-Ph
1-1632	cHex	2-nPent-Ph
1-1633	cHept	2-nPent-Ph
1-1634	oxi	2-nPent-Ph

TABLE 1-continued



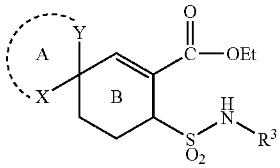
Compound No.	X, Y	R^3
1-1635	oxe	2-nPent-Ph
1-1636	oxo	2-nPent-Ph
1-1637	oxa	2-nPent-Ph
1-1638	dioxo	2-nPent-Ph
1-1639	dioxa	2-nPent-Ph
1-1640	dioxe	2-nPent-Ph
1-1641	dithio	2-nPent-Ph
1-1642	dithia	2-nPent-Ph
1-1643	ring 1	2-nPent-Ph
1-1644	ring 2	2-nPent-Ph
1-1645	oxathio	2-nPent-Ph
1-1646	oxathia	2-nPent-Ph
1-1647	ozl	2-nPent-Ph
1-1648	ozn	2-nPent-Ph
1-1649	tzl	2-nPent-Ph
1-1650	tzn	2-nPent-Ph
1-1651	3-HM-cPent	2-nPent-Ph
1-1652	4-HM-dioxo	2-nPent-Ph
1-1653	4-HM-dithio	2-nPent-Ph
1-1654	4-HM-oxathio	2-nPent-Ph
1-1655	3,4-diHM-cPent	2-nPent-Ph
1-1656	4,5-diHM-dioxo	2-nPent-Ph
1-1657	4,5-diHM-dithio	2-nPent-Ph
1-1658	4,5-diHM-oxathio	2-nPent-Ph
1-1659	3,4-diHE-cPent	2-nPent-Ph
1-1660	4,5-diHE-dioxo	2-nPent-Ph
1-1661	4,5-diHE-dithio	2-nPent-Ph
1-1662	4,5-diHE-oxathio	2-nPent-Ph
1-1663	3-HE-cPent	2-nPent-Ph
1-1664	4-HE-dioxo	2-nPent-Ph
1-1665	4-HE-dithio	2-nPent-Ph
1-1666	4-HE-oxathio	2-nPent-Ph
1-1667	3-HP-cPent	2-nPent-Ph
1-1668	4-HP-dioxo	2-nPent-Ph
1-1669	4-HP-dithio	2-nPent-Ph
1-1670	4-HP-oxathio	2-nPent-Ph
1-1671	3-HB-cPent	2-nPent-Ph
1-1672	4-HB-dioxo	2-nPent-Ph
1-1673	4-HB-dithio	2-nPent-Ph
1-1674	4-HB-oxathio	2-nPent-Ph
1-1675	ring 3	2-nPent-Ph
1-1676	ring 4	2-nPent-Ph
1-1677	ring 5	2-nPent-Ph
1-1678	ring 6	2-nPent-Ph
1-1679	ring 7	2-nPent-Ph
1-1680	ring 8	2-nPent-Ph
1-1681	ring 9	2-nPent-Ph
1-1682	ring 10	2-nPent-Ph
1-1683	3,4-diCH_2NHAc-cPent	2-nPent-Ph
1-1684	4,5-diCH_2NHAc-dioxo	2-nPent-Ph
1-1685	4,5-diCH_2NHAc-dithio	2-nPent-Ph
1-1686	4,5-diCH_2NHAc-oxathio	2-nPent-Ph
1-1687	ring 11	2-nPent-Ph
1-1688	ring 12	2-nPent-Ph
1-1689	ring 13	2-nPent-Ph
1-1690	ring 14	2-nPent-Ph
1-1691	4-OH-cHex	2-nPent-Ph
1-1692	5-OH-dioxa	2-nPent-Ph
1-1693	5-OH-dithia	2-nPent-Ph
1-1694	5-OH-oxathia	2-nPent-Ph
1-1695	4-NHAc-cHex	2-nPent-Ph
1-1696	5-NHAc-dioxa	2-nPent-Ph
1-1697	5-NHAc-dithia	2-nPent-Ph
1-1698	5-NHAc-oxathia	2-nPent-Ph
1-1699	4,4-diMe-cHex	2-nPent-Ph
1-1700	5,5-diMe-dioxa	2-nPent-Ph
1-1701	5,5-diMe-dithia	2-nPent-Ph
1-1702	5,5-diMe-oxathia	2-nPent-Ph

TABLE 1-continued



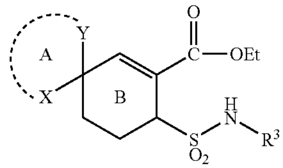
Compound No.	X, Y	R^3
1-1703	4,4-diHM-cHex	2-nPent-Ph
1-1704	5,5-diHM-dioxa	2-nPent-Ph
1-1705	5,5-diHM-dithia	2-nPent-Ph
1-1706	5,5-diHM-oxathia	2-nPent-Ph
1-1707	ring 15	2-nPent-Ph
1-1708	ring 16	2-nPent-Ph
1-1709	ring 17	2-nPent-Ph
1-1710	ring 18	2-nPent-Ph
1-1711	4,4-diCO_2Et-cHex	2-nPent-Ph
1-1712	5,5-diCO_2Et-dioxa	2-nPent-Ph
1-1713	5,5-diCO_2Et-dithia	2-nPent-Ph
1-1714	5,5-diCO_2Et-oxathia	2-nPent-Ph
1-1715	O=	4-F-2-nPent-Ph
1-1716	S=	4-F-2-nPent-Ph
1-1717	cPr	4-F-2-nPent-Ph
1-1718	cBu	4-F-2-nPent-Ph
1-1719	cPent	4-F-2-nPent-Ph
1-1720	cHex	4-F-2-nPent-Ph
1-1721	cHept	4-F-2-nPent-Ph
1-1722	oxi	4-F-2-nPent-Ph
1-1723	oxe	4-F-2-nPent-Ph
1-1724	oxo	4-F-2-nPent-Ph
1-1725	oxa	4-F-2-nPent-Ph
1-1726	dioxo	4-F-2-nPent-Ph
1-1727	dioxa	4-F-2-nPent-Ph
1-1728	dioxe	4-F-2-nPent-Ph
1-1729	dithio	4-F-2-nPent-Ph
1-1730	dithia	4-F-2-nPent-Ph
1-1731	ring 1	4-F-2-nPent-Ph
1-1732	ring 2	4-F-2-nPent-Ph
1-1733	oxathio	4-F-2-nPent-Ph
1-1734	oxathia	4-F-2-nPent-Ph
1-1735	ozl	4-F-2-nPent-Ph
1-1736	ozn	4-F-2-nPent-Ph
1-1737	tzl	4-F-2-nPent-Ph
1-1738	tzn	4-F-2-nPent-Ph
1-1739	3-HM-cPent	4-F-2-nPent-Ph
1-1740	4-HM-dioxo	4-F-2-nPent-Ph
1-1741	4-HM-dithio	4-F-2-nPent-Ph
1-1742	4-HM-oxathio	4-F-2-nPent-Ph
1-1743	3,4-diHM-cPent	4-F-2-nPent-Ph
1-1744	4,5-diHM-dioxo	4-F-2-nPent-Ph
1-1745	4,5-diHM-dithio	4-F-2-nPent-Ph
1-1746	4,5-diHM-oxathio	4-F-2-nPent-Ph
1-1747	3,4-diHE-cPent	4-F-2-nPent-Ph
1-1748	4,5-diHE-dioxo	4-F-2-nPent-Ph
1-1749	4,5-diHE-dithio	4-F-2-nPent-Ph
1-1750	4,5-diHE-oxathio	4-F-2-nPent-Ph
1-1751	3-HE-cPent	4-F-2-nPent-Ph
1-1752	4-HE-dioxo	4-F-2-nPent-Ph
1-1753	4-HE-dithio	4-F-2-nPent-Ph
1-1754	4-HE-oxathio	4-F-2-nPent-Ph
1-1755	3-HP-cPent	4-F-2-nPent-Ph
1-1756	4-HP-dioxo	4-F-2-nPent-Ph
1-1757	4-HP-dithio	4-F-2-nPent-Ph
1-1758	4-HP-oxathio	4-F-2-nPent-Ph
1-1759	3-HB-cPent	4-F-2-nPent-Ph
1-1760	4-HB-dioxo	4-F-2-nPent-Ph
1-1761	4-HB-dithio	4-F-2-nPent-Ph
1-1762	4-HB-oxathio	4-F-2-nPent-Ph
1-1763	ring 3	4-F-2-nPent-Ph
1-1764	ring 4	4-F-2-nPent-Ph
1-1765	ring 5	4-F-2-nPent-Ph
1-1766	ring 6	4-F-2-nPent-Ph
1-1767	ring 7	4-F-2-nPent-Ph
1-1768	ring 8	4-F-2-nPent-Ph
1-1769	ring 9	4-P-2-nPent-Ph
1-1770	ring 10	4-F-2-nPent-Ph

TABLE 1-continued



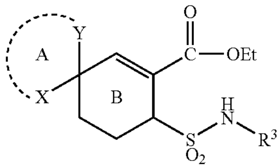
Compound No.	X, Y	R^3
1-1771	3,4-diCH_2NHAc-cPent	4-F-2-nPent-Ph
1-1772	4,5-diCH_2NHAc-dioxo	4-F-2-nPent-Ph
1-1773	4,5-diCH_2NHAc-dithio	4-F-2-nPent-Ph
1-1774	4,5-diCH_2NHAc-oxathio	4-F-2-nPent-Ph
1-1775	ring 11	4-F-2-nPent-Ph
1-1776	ring 12	4-F-2-nPent-Ph
1-1777	ring 13	4-F-2-nPent-Ph
1-1778	ring 14	4-F-2-nPent-Ph
1-1779	4-OH-cHex	4-F-2-nPent-Ph
1-1780	5-OH-dioxa	4-F-2-nPent-Ph
1-1781	5-OH-dithia	4-F-2-nPent-Ph
1-1782	5-OH-oxathia	4-F-2-nPent-Ph
1-1783	4-NHAc-cHex	4-F-2-nPent-Ph
1-1784	5-NHAc-dioxa	4-F-2-nPent-Ph
1-1785	5-NHAc-dithia	4-F-2-nPent-Ph
1-1786	5-NHAc-oxathia	4-F-2-nPent-Ph
1-1787	4,4-diMe-cHex	4-F-2-nPent-Ph
1-1788	5,5-diMe-dioxa	4-F-2-nPent-Ph
1-1789	5,5-diMe-dithia	4-F-2-nPent-Ph
1-1790	5,5-diMe-oxathia	4-F-2-nPent-Ph
1-1791	4,4-diHM-cHex	4-F-2-nPent-Ph
1-1792	5,5-diHM-dioxa	4-F-2-nPent-Ph
1-1793	5,5-diHM-dithia	4-F-2-nPent-Ph
1-1794	5,5-diHM-oxathia	4-F-2-nPent-Ph
1-1795	ring 15	4-F-2-nPent-Ph
1-1796	ring 16	4-F-2-nPent-Ph
1-1797	ring 17	4-F-2-nPent-Ph
1-1798	ring 18	4-F-2-nPent-Ph
1-1799	4,4-diCO_2Et-cHex	4-F-2-nPent-Ph
1-1800	5,5-diCO_2Et-dioxa	4-F-2-nPent-Ph
1-1801	5,5-diCO_2Et-dithia	4-F-2-nPent-Ph
1-1802	5,5-diCO_2Et-oxathia	4-F-2-nPent-Ph
1-1803	O=	2-nOct-Ph
1-1804	S=	2-nOct-Ph
1-1805	cPr	2-nOct-Ph
1-1806	cBu	2-nOct-Ph
1-1807	cPent	2-nOct-Ph
1-1808	cHex	2-nOct-Ph
1-1809	cHept	2-nOct-Ph
1-1810	oxi	2-nOct-Ph
1-1811	oxe	2-nOct-Ph
1-1812	oxo	2-nOct-Ph
1-1813	oxa	2-nOct-Ph
1-1814	dioxo	2-nOct-Ph
1-1815	dioxa	2-nOct-Ph
1-1816	dioxe	2-nOct-Ph
1-1817	dithio	2-nOct-Ph
1-1818	dithia	2-nOct-Ph
1-1819	ring 1	2-nOct-Ph
1-1820	ring 2	2-nOct-Ph
1-1821	oxathio	2-nOct-Ph
1-1822	oxathia	2-nOct-Ph
1-1823	ozl	2-nOct-Ph
1-1824	ozn	2-nOct-Ph
1-1825	tzl	2-nOct-Ph
1-1826	tzn	2-nOct-Ph
1-1827	3-HM-cPent	2-nOct-Ph
1-1828	4-HM-dioxo	2-nOct-Ph
1-1829	4-HM-dithio	2-nOct-Ph
1-1830	4-HM-oxathio	2-nOct-Ph
1-1831	3,4-diHM-cPent	2-nOct-Ph
1-1832	4,5-diHM-dioxo	2-nOct-Ph
1-1833	4,5-diHM-dithio	2-nOct-Ph
1-1834	4,5-diHM-oxathio	2-nOct-Ph
1-1835	3,4-diHE-cPent	2-nOct-Ph
1-1836	4,5-diHE-dioxo	2-nOct-Ph
1-1837	4,5-diHE-dithio	2-nOct-Ph
1-1838	4,5-diHE-oxathio	2-nOct-Ph

TABLE 1-continued



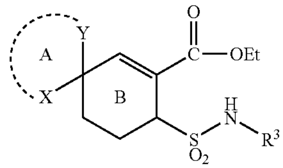
Compound No.	X, Y	R^3
1-1839	3-HE-cPent	2-nOct-Ph
1-1840	4-HE-dioxo	2-nOct-Ph
1-1841	4-HE-dithio	2-nOct-Ph
1-1842	4-HE-oxathio	2-nOct-Ph
1-1843	3-HP-cPent	2-nOct-Ph
1-1844	4-HP-dioxo	2-nOct-Ph
1-1845	4-HP-dithio	2-nOct-Ph
1-1846	4-HP-oxathio	2-nOct-Ph
1-1847	3-HB-cPent	2-nOct-Ph
1-1848	4-HB-dioxo	2-nOct-Ph
1-1849	4-HB-dithio	2-nOct-Ph
1-1850	4-HB-oxathio	2-nOct-Ph
1-1851	ring 3	2-nOct-Ph
1-1852	ring 4	2-nOct-Ph
1-1853	ring 5	2-nOct-Ph
1-1854	ring 6	2-nOct-Ph
1-1855	ring 7	2-nOct-Ph
1-1856	ring 8	2-nOct-Ph
1-1857	ring 9	2-nOct-Ph
1-1858	ring 10	2-nOct-Ph
1-1859	3,4-diCH_2NHAc-cPent	2-nOct-Ph
1-1860	4,5-diCH_2NHAc-dioxo	2-nOct-Ph
1-1861	4,5-diCH_2NHAc-dithio	2-nOct-Ph
1-1862	4,5-diCH_2NHAc-oxathio	2-nOct-Ph
1-1863	ring 11	2-nOct-Ph
1-1864	ring 12	2-nOct-Ph
1-1865	ring 13	2-nOct-Ph
1-1866	ring 14	2-nOct-Ph
1-1867	4-OH-cHex	2-nOct-Ph
1-1868	5-OH-dioxa	2-nOct-Ph
1-1869	5-OH-dithia	2-nOct-Ph
1-1870	5-OH-oxathia	2-nOct-Ph
1-1871	4-NHAc-cHex	2-nOct-Ph
1-1872	5-NHAc-dioxa	2-nOct-Ph
1-1873	5-NHAc-dithia	2-nOct-Ph
1-1874	5-NHAc-oxathia	2-nOct-Ph
1-1875	4,4-diMe-cHex	2-nOct-Ph
1-1876	5,5-diMe-dioxa	2-nOct-Ph
1-1877	5,5-diMe-dithia	2-nOct-Ph
1-1878	5,5-diMe-oxathia	2-nOct-Ph
1-1879	4,4-diHM-cHex	2-nOct-Ph
1-1880	5,5-diHM-dioxa	2-nOct-Ph
1-1881	5,5-diHM-dithia	2-nOct-Ph
1-1882	5,5-diHM-oxathia	2-nOct-Ph
1-1883	ring 15	2-nOct-Ph
1-1884	ring 16	2-nOct-Ph
1-1885	ring 17	2-nOct-Ph
1-1886	ring 18	2-nOct-Ph
1-1887	4,4-diCO_2Et-cHex	2-nOct-Ph
1-1888	5,5-diCO_2Et-dioxa	2-nOct-Ph
1-1889	5,5-diCO_2Et-dithia	2-nOct-Ph
1-1890	5,5-diCO_2Et-oxathia	2-nOct-Ph
1-1891	O=	4-F-2-nOct-Ph
1-1892	S=	4-F-2-nOct-Ph
1-1893	cPr	4-F-2-nOct-Ph
1-1894	cBu	4-F-2-nOct-Ph
1-1895	cPent	4-F-2-nOct-Ph
1-1896	cHex	4-F-2-nOct-Ph
1-1897	cHept	4-F-2-nOct-Ph
1-1898	oxi	4-F-2-nOct-Ph
1-1899	oxe	4-F-2-nOct-Ph
1-1900	oxo	4-F-2-nOct-Ph
1-1901	oxa	4-F-2-nOct-Ph
1-1902	diaxo	4-F-2-nOct-Ph
1-1903	dioxa	4-F-2-nOct-Ph
1-1904	dioxe	4-F-2-nOct-Ph
1-1905	dithio	4-F-2-nOct-Ph
1-1906	dithia	4-F-2-nOct-Ph

TABLE 1-continued



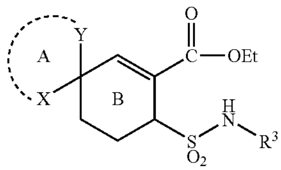
Compound No.	X, Y	R^3
1-1907	ring 1	4-F-2-nOct-Ph
1-1908	ring 2	4-F-2-nOct-Ph
1-1909	oxathio	4-F-2-nOct-Ph
1-1910	oxathia	4-F-2-nOct-Ph
1-1911	ozl	4-F-2-nOct-Ph
1-1912	ozn	4-F-2-nOct-Ph
1-1913	tzl	4-F-2-nOct-Ph
1-1914	tzn	4-F-2-nOct-Ph
1-1915	3-HM-cPent	4-F-2-nOct-Ph
1-1916	4-HM-dioxo	4-F-2-nOct-Ph
1-1917	4-HM-dithio	4-F-2-nOct-Ph
1-1918	4-HM-oxathio	4-F-2-nOct-Ph
1-1919	3,4-diHM-cPent	4-F-2-nOct-Ph
1-1920	4,5-diHM-dioxo	4-F-2-nOct-Ph
1-1921	4,5-diHM-dithio	4-F-2-nOct-Ph
1-1922	4,5-diHM-oxathio	4-F-2-nOct-Ph
1-1923	3,4-diHE-cPent	4-F-2-nOct-Ph
1-1924	4,5-diHE-dioxo	4-F-2-nOct-Ph
1-1925	4,5-diHE-dithio	4-F-2-nOct-Ph
1-1926	4,5-diHE-oxathio	4-F-2-nOct-Ph
1-1927	3-HE-cPent	4-F-2-nOct-Ph
1-1928	4-HE-dioxo	4-F-2-nOct-Ph
1-1929	4-HE-dithio	4-F-2-nOct-Ph
1-1930	4-HE-oxathio	4-F-2-nOct-Ph
1-1931	3-HP-cPent	4-F-2-nOct-Ph
1-1932	4-HP-dioxo	4-F-2-nOct-Ph
1-1933	4-HP-dithio	4-F-2-nOct-Ph
1-1934	4-HP-oxathio	4-F-2-nOct-Ph
1-1935	3-HB-cPent	4-F-2-nOct-Ph
1-1936	4-HB-dioxo	4-F-2-nOct-Ph
1-1937	4-HB-dithio	4-F-2-nOct-Ph
1-1938	4-HB-oxathio	4-F-2-nOct-Ph
1-1939	ring 3	4-F-2-nOct-Ph
1-1940	ring 4	4-F-2-nOct-Ph
1-1941	ring 5	4-F-2-nOct-Ph
1-1942	ring 6	4-F-2-nOct-Ph
1-1943	ring 7	4-F-2-nOct-Ph
1-1944	ring 8	4-F-2-nOct-Ph
1-1945	ring 9	4-F-2-nOct-Ph
1-1946	ring 10	4-F-2-nOct-Ph
1-1947	3,4-diCH_2NHAc-cPent	4-F-2-nOct-Ph
1-1948	4,5-diCH_2NHAc-dioxo	4-F-2-nOct-Ph
1-1949	4,5-diCH_2NHAc-dithio	4-F-2-nOct-Ph
1-1950	4,5-diCH_2NHAc-oxathio	4-F-2-nOct-Ph
1-1951	ring 11	4-F-2-nOct-Ph
1-1952	ring 12	4-F-2-nOct-Ph
1-1953	ring 13	4-F-2-nOct-Ph
1-1954	ring 14	4-F-2-nOct-Ph
1-1955	4-OH-cHex	4-F-2-nOct-Ph
1-1956	5-OH-dioxa	4-F-2-nOct-Ph
1-1957	5-OH-dithia	4-F-2-nOct-Ph
1-1958	5-OH-oxathia	4-F-2-nOct-Ph
1-1959	4-NHAc-cHex	4-F-2-nOct-Ph
1-1960	5-NHAc-dioxa	4-F-2-nOct-Ph
1-1961	5-NHAc-dithia	4-F-2-nOct-Ph
1-1962	5-NHAc-oxathia	4-F-2-nOct-Ph
1-1963	4,4-diMe-cHex	4-F-2-nOct-Ph
1-1964	5,5-diMe-dioxa	4-F-2-nOct-Ph
1-1965	5,5-diMe-dithia	4-F-2-nOct-Ph
1-1966	5,5-diMe-oxathia	4-F-2-nOct-Ph
1-1967	4,4-diHM-cHex	4-F-2-nOct-Ph
1-1968	5,5-diHM-dioxa	4-F-2-nOct-Ph
1-1969	5,5-diHM-dithia	4-F-2-nOct-Ph
1-1970	5,5-diHM-oxathia	4-F-2-nOct-Ph
1-1971	ring 15	4-F-2-nOct-Ph
1-1972	ring 16	4-F-2-nOct-Ph
1-1973	ring 17	4-F-2-nOct-Ph
1-1974	ring 18	4-F-2-nOct-Ph

TABLE 1-continued



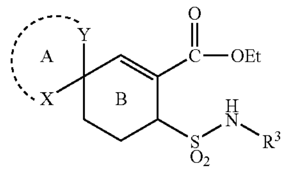
Compound No.	X, Y	R^3
1-1975	4,4-diCO_2Et-cHex	4-F-2-nOct-Ph
1-1976	5,5-diCO_2Et-dioxa	4-F-2-nOct-Ph
1-1977	5,5-diCO_2Et-dithia	4-F-2-nOct-Ph
1-1978	O=	2-nPr-Ph
1-1979	S=	2-nPr-Ph
1-1980	cPr	2-nPr-Ph
1-1981	cBu	2-nPr-Ph
1-1982	cPent	2-nPr-Ph
1-1983	cHex	2-nPr-Ph
1-1984	cHept	2-nPr-Ph
1-1985	oxi	2-nPr-Ph
1-1986	oxe	2-nPr-Ph
1-1987	oxo	2-nPr-Ph
1-1988	oxa	2-nPr-Ph
1-1989	dioxo	2-nPr-Ph
1-1990	dioxa	2-nPr-Ph
1-1991	dioxe	2-nPr-Ph
1-1992	dithio	2-nPr-Ph
1-1993	dithia	2-nPr-Ph
1-1994	ring 1	2-nPr-Ph
1-1995	ring 2	2-nPr-Ph
1-1996	oxathio	2-nPr-Ph
1-1997	oxathia	2-nPr-Ph
1-1998	ozl	2-nPr-Ph
1-1999	ozn	2-nPr-Ph
1-2000	tzl	2-nPr-Ph
1-2001	tzn	2-nPr-Ph
1-2002	3-HM-cPent	2-nPr-Ph
1-2003	4-HM-dioxo	2-nPr-Ph
1-2004	4-HM-dithio	2-nPr-Ph
1-2005	4-HM-oxathio	2-nPr-Ph
1-2006	3,4-diHM-cPent	2-nPr-Ph
1-2007	4,5-diHM-dioxo	2-nPr-Ph
1-2008	4,5-diHM-dithio	2-nPr-Ph
1-2009	4,5-diHM-oxathio	2-nPr-Ph
1-2010	3,4-diHE-cPent	2-nPr-Ph
1-2011	4,5-diHE-dioxo	2-nPr-Ph
1-2012	4,5-diHE-dithio	2-nPr-Ph
1-2013	4,5-diHE-oxathio	2-nPr-Ph
1-2014	3-HE-cPent	2-nPr-Ph
1-2015	4-HE-dioxo	2-nPr-Ph
1-2016	4-HE-dithio	2-nPr-Ph
1-2017	4-HE-oxathio	2-nPr-Ph
1-2018	3-HP-cPent	2-nPr-Ph
1-2019	4-HP-dioxo	2-nPr-Ph
1-2020	4-HP-dithio	2-nPr-Ph
1-2021	4-HP-oxathio	2-nPr-Ph
1-2022	3-HB-cPent	2-nPr-Ph
1-2023	4-HB-dioxo	2-nPr-Ph
1-2024	4-HB-dithio	2-nPr-Ph
1-2025	4-HB-oxathio	2-nPr-Ph
1-2026	ring 3	2-nPr-Ph
1-2027	ring 4	2-nPr-Ph
1-2028	ring 5	2-nPr-Ph
1-2029	ring 6	2-nPr-Ph
1-2030	ring 7	2-nPr-Ph
1-2031	ring 8	2-nPr-Ph
1-2032	ring 9	2-nPr-Ph
1-2033	ring 10	2-nPr-Ph
1-2034	3,4-diCH_2NHAc-cPent	2-nPr-Ph
1-2035	4,5-diCH_2NHAc-dioxo	2-nPr-Ph
1-2036	4,5-diCH_2NHAc-dithio	2-nPr-Ph
1-2037	4,5-diCH_2NHAc-oxathio	2-nPr-Ph
1-2038	ring 11	2-nPr-Ph
1-2039	ring 12	2-nPr-Ph
1-2040	ring 13	2-nPr-Ph
1-2041	ring 14	2-nPr-Ph
1-2042	4-OH-cHex	2-nPr-Ph

TABLE 1-continued



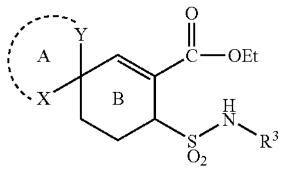
Compound No.	X, Y	R^3
1-2043	5-OH-dioxa	2-nPr-Ph
1-2044	5-OH-dithia	2-nPr-Ph
1-2045	5-OH-oxathia	2-nPr-Ph
1-2046	4-NHAc-cHex	2-nPr-Ph
1-2047	5-NHAc-dioxa	2-nPr-Ph
1-2048	5-NHAc-dithia	2-nPr-Ph
1-2049	5-NHAc-oxathia	2-nPr-Ph
1-2050	4,4-diMe-cHex	2-nPr-Ph
1-2051	5,5-diMe-dioxa	2-nPr-Ph
1-2052	5,5-diMe-dithia	2-nPr-Ph
1-2053	5,5-diMe-oxathia	2-nPr-Ph
1-2054	4,4-diHM-cHex	2-nPr-Ph
1-2055	5,5-diHM-dioxa	2-nPr-Ph
1-2056	5,5-diHM-dithia	2-nPr-Ph
1-2057	5,5-diHM-oxathia	2-nPr-Ph
1-2058	ring 15	2-nPr-Ph
1-2059	ring 16	2-nPr-Ph
1-2060	ring 17	2-nPr-Ph
1-2061	ring 18	2-nPr-Ph
1-2062	4,4-diCO_2Et-cHex	2-nPr-Ph
1-2063	5,5-diCO_2Et-dioxa	2-nPr-Ph
1-2064	5,5-diCO_2Et-dithia	2-nPr-Ph
1-2065	5,5-diCO_2Et-oxathia	2-nPr-Ph
1-2066	O═	4-F-2-nPr-Ph
1-2067	S═	4-F-2-nPr-Ph
1-2068	cPr	4-F-2-nPr-Ph
1-2069	cBu	4-F-2-nPr-Ph
1-2070	cPent	4-F-2-nPr-Ph
1-2071	cHex	4-F-2-nPr-Ph
1-2072	cHept	4-F-2-nPr-Ph
1-2073	oxi	4-F-2-nPr-Ph
1-2074	oxe	4-F-2-nPr-Ph
1-2075	oxo	4-F-2-nPr-Ph
1-2076	oxa	4-F-2-nPr-Ph
1-2077	dioxo	4-F-2-nPr-Ph
1-2078	dioxa	4-F-2-nPr-Ph
1-2079	dioxe	4-F-2-nPr-Ph
1-2080	dithio	4-F-2-nPr-Ph
1-2081	dithia	4-F-2-nPr-Ph
1-2082	ring 1	4-F-2-nPr-Ph
1-2083	ring 2	4-F-2-nPr-Ph
1-2084	oxathio	4-F-2-nPr-Ph
1-2085	oxathia	4-F-2-nPr-Ph
1-2086	ozl	4-F-2-nPr-Ph
1-2087	ozn	4-F-2-nPr-Ph
1-2088	tzl	4-F-2-nPr-Ph
1-2089	tzn	4-F-2-nPr-Ph
1-2090	3-HM-cPent	4-F-2-nPr-Ph
1-2091	4-HM-dioxo	4-F-2-nPr-Ph
1-2092	4-HM-dithio	4-F-2-nPr-Ph
1-2093	4-HM-oxathio	4-F-2-nPr-Ph
1-2094	3,4-diHM-cPent	4-F-2-nPr-Ph
1-2095	4,5-diHM-dioxo	4-F-2-nPr-Ph
1-2096	4,5-diHM-dithio	4-F-2-nPr-Ph
1-2097	4,5-diHM-oxathio	4-F-2-nPr-Ph
1-2098	3,4-diHE-cPent	4-F-2-nPr-Ph
1-2099	4,5-diHE-dioxo	4-F-2-nPr-Ph
1-2100	4,5-diHE-dithio	4-F-2-nPr-Ph
1-2101	4,5-diHE-oxathio	4-F-2-nPr-Ph
1-2102	3-HE-cPent	4-F-2-nPr-Ph
1-2103	4-HE-dioxo	4-F-2-nPr-Ph
1-2104	4-HE-dithio	4-F-2-nPr-Ph
1-2105	4-HE-oxathio	4-F-2-nPr-Ph
1-2106	3-HP-cPent	4-F-2-nPr-Ph
1-2107	4-HP-dioxo	4-F-2-nPr-Ph
1-2108	4-HP-dithio	4-F-2-nPr-Ph
1-2109	4-HP-oxathio	4-F-2-nPr-Ph
1-2110	3-HB-cPent	4-F-2-nPr-Ph

TABLE 1-continued



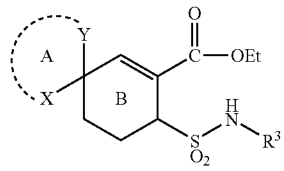
Compound No.	X, Y	R^3
1-2111	4-HB-dioxo	4-F-2-nPr-Ph
1-2112	4-HB-dithio	4-F-2-nPr-Ph
1-2113	4-HB-oxathio	4-F-2-nPr-Ph
1-2114	ring 3	4-F-2-nPr-Ph
1-2115	ring 4	4-F-2-nPr-Ph
1-2116	ring 5	4-F-2-nPr-Ph
1-2117	ring 6	4-F-2-nPr-Ph
1-2118	ring 7	4-F-2-nPr-Ph
1-2119	ring 8	4-F-2-nPr-Ph
1-2120	ring 9	4-F-2-nPr-Ph
1-2121	ring 10	4-F-2-nPr-Ph
1-2122	3,4-diCH_2NHAc-cPent	4-F-2-nPr-Ph
1-2123	4,5-diCH_2NHAc-dioxo	4-F-2-nPr-Ph
1-2124	4,5-diCH_2NHAc-dithio	4-F-2-nPr-Ph
1-2125	4,5-diCH_2NHAc-oxathio	4-F-2-nPr-Ph
1-2126	ring 11	4-F-2-nPr-Ph
1-2127	ring 12	4-F-2-nPr-Ph
1-2128	ring 13	4-F-2-nPr-Ph
1-2129	ring 14	4-F-2-nPr-Ph
1-2130	4-OH-cHex	4-F-2-nPr-Ph
1-2131	5-OH-dioxa	4-F-2-nPr-Ph
1-2132	5-OH-dithia	4-F-2-nPr-Ph
1-2133	5-OH-oxathia	4-F-2-nPr-Ph
1-2134	4-NHAc-cHex	4-F-2-nPr-Ph
1-2135	5-NHAc-dioxa	4-F-2-nPr-Ph
1-2136	5-NHAc-dithia	4-F-2-nPr-Ph
1-2137	5-NHAc-oxathia	4-F-2-nPr-Ph
1-2138	4,4-diMe-cHex	4-F-2-nPr-Ph
1-2139	5,5-diMe-dioxa	4-F-2-nPr-Ph
1-2140	5,5-diMe-dithia	4-F-2-nPr-Ph
1-2141	5,5-diMe-oxathia	4-F-2-nPr-Ph
1-2142	4,4-diHM-cHex	4-F-2-nPr-Ph
1-2143	5,5-diHM-dioxa	4-F-2-nPr-Ph
1-2144	5,5-diHM-dithia	4-F-2-nPr-Ph
1-2145	5,5-diHM-oxathia	4-F-2-nPr-Ph
1-2146	ring 15	4-F-2-nPr-Ph
1-2147	ring 16	4-F-2-nPr-Ph
1-2148	ring 17	4-F-2-nPr-Ph
1-2149	ring 18	4-F-2-nPr-Ph
1-2150	4,4-diCO_2Et-cHex	4-F-2-nPr-Ph
1-2151	5,5-diCO_2Et-dioxa	4-F-2-nPr-Ph
1-2152	5,5-diCO_2Et-dithia	4-F-2-nPr-Ph
1-2153	5,5-diCO_2Et-oxathia	4-F-2-nPr-Ph
1-2154	ring 19	2-Cl-Ph
1-2155	ring 20	2-Cl-Ph
1-2156	ring 21	2-Cl-Ph
1-2157	ring 19	2-Br-Ph
1-2158	ring 20	2-Br-Ph
1-2159	ring 21	2-Br-Ph
1-2160	ring 19	2-Cl-6-Me-Ph
1-2161	ring 20	2-Cl-6-Me-Ph
1-2162	ring 21	2-Cl-6-Me-Ph
1-2163	ring 19	2-Cl-4-F-Ph
1-2164	ring 20	2-Cl-4-F-Ph
1-2165	ring 21	2-Cl-4-F-Ph
1-2166	ring 19	2,4-diF
1-2167	ring 20	2,4-diF
1-2168	ring 21	2,4-diF
1-2169	ring 19	2-Br-4-F-Ph
1-2170	ring 20	2-Br-4-F-Ph
1-2171	ring 21	2-Br-4-F-Ph
1-2172	ring 19	2-nBu-4-F-Ph
1-2173	ring 20	2-nBu-4-F-Ph
1-2174	ring 21	2-nBu-4-F-Ph
1-2175	ring 19	2-nPent-Ph
1-2176	ring 20	2-nPent-Ph
1-2177	ring 21	2-nPent-Ph
1-2178	ring 19	4-F-2-nPent-Ph

TABLE 1-continued



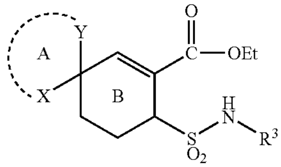
Compound No.	X, Y	R^3
1-2179	ring 20	4-F-2-nPent-Ph
1-2180	ring 21	4-F-2-nPent-Ph
1-2181	ring 19	2-nHex-Ph
1-2182	ring 20	2-nHex-Ph
1-2183	ring 21	2-nHex-Ph
1-2184	ring 19	4-F-2-nHex-Ph
1-2185	ring 20	4-F-2-nHex-Ph
1-2186	ring 21	4-F-2-nHex-Ph
1-2187	ring 19	2-nHept-Ph
1-2188	ring 20	2-nHept-Ph
1-2189	ring 21	2-nHept-Ph
1-2190	ring 19	4-F-2-nHept-Ph
1-2191	ring 20	4-F-2-nHept-Ph
1-2192	ring 21	4-F-2-nHept-Ph
1-2193	ring 19	2-nOct-Ph
1-2194	ring 20	2-nOct-Ph
1-2195	ring 21	2-nOct-Ph
1-2196	ring 19	4-F-2-nOct-Ph
1-2197	ring 20	4-F-2-nOct-Ph
1-2198	ring 21	4-F-2-nOct-Ph
1-2199	ring 19	Ph
1-2200	ring 20	Ph
1-2201	ring 21	Ph
1-2202	ring 19	4-F-Ph
1-2203	ring 20	4-F-Ph
1-2204	ring 21	4-F-Ph
1-2205	ring 19	2-Cl-4-Me-Ph
1-2206	ring 20	2-Cl-4-Me-Ph
1-2207	ring 21	2-Cl-4-Me-Ph
1-2208	ring 19	2-nBu-Ph
1-2209	ring 20	2-nBu-Ph
1-2210	ring 21	2-nBu-Ph
1-2211	ring 19	2-nPr-Ph
1-2212	ring 20	2-nPr-Ph
1-2213	ring 21	2-nPr-Ph
1-2214	ring 19	4-F-2-nPr-Ph
1-2215	ring 20	4-F-2-nPr-Ph
1-2216	ring 21	4-F-2-nPr-Ph
1-2217	dioxo	2-F-Ph
1-2218	4-HM-dioxo	2-F-Ph
1-2219	4,5-diHM-dioxo	2-F-Ph
1-2220	4,5-diHE-dioxo	2-F-Ph
1-2221	ring 19	2-F-Ph
1-2222	ring 20	2-F-Ph
1-2223	ring 21	2-F-Ph
1-2224	dioxo	2-I-Ph
1-2225	4-HM-dioxo	2-I-Ph
1-2226	4,5-diHM-dioxo	2-I-Ph
1-2227	4,5-diHE-dioxo	2-I-Ph
1-2228	ring 19	2-I-Ph
1-2229	ring 20	2-I-Ph
1-2230	ring 21	2-I-Ph
1-2231	dioxo	4-Cl-Ph
1-2232	4-HM-dioxo	4-Cl-Ph
1-2233	4,5-diHM-dioxo	4-Cl-Ph
1-2234	4,5-diHE-dioxo	4-Cl-Ph
1-2235	ring 19	4-Cl-Ph
1-2236	ring 20	4-Cl-Ph
1-2237	ring 21	4-Cl-Ph
1-2238	dioxo	2-Me-Ph
1-2239	4-HM-dioxo	2-Me-Ph
1-2240	4,5-diHM-dioxo	2-Me-Ph
1-2241	4,5-diHE-dioxo	2-Me-Ph
1-2242	ring 19	2-Me-Ph
1-2243	ring 20	2-Me-Ph
1-2244	ring 21	2-Me-Ph
1-2245	dioxo	2-Et-Ph
1-2246	4-HM-dioxo	2-Et-Ph

TABLE 1-continued



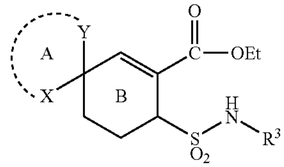
Compound No.	X, Y	R^3
1-2247	4,5-diHM-dioxo	2-Et-Ph
1-2248	4,5-diHE-dioxo	2-Et-Ph
1-2249	ring 19	2-Et-Ph
1-2250	ring 20	2-Et-Ph
1-2251	ring 21	2-Et-Ph
1-2252	dioxo	2-C≡CH-Ph
1-2253	4-HM-dioxo	2-C≡CH-Ph
1-2254	4,5-diHM-dioxo	2-C≡CH-Ph
1-2255	4,5-diHE-dioxo	2-C≡CH-Ph
1-2256	ring 19	2-C≡CH-Ph
1-2257	ring 20	2-C≡CH-Ph
1-2258	ring 21	2-C≡CH-Ph
1-2259	dioxo	2-iPr-Ph
1-2260	4-HM-dioxo	2-iPr-Ph
1-2261	4,5-diHM-dioxo	2-iPr-Ph
1-2262	4,5-diHE-dioxo	2-iPr-Ph
1-2263	ring 19	2-iPr-Ph
1-2264	ring 20	2-iPr-Ph
1-2265	ring 21	2-iPr-Ph
1-2266	dioxo	2-tBu-Ph
1-2267	4-HM-dioxo	2-tBu-Ph
1-2268	4,5-diHM-dioxo	2-tBu-Ph
1-2269	4,5-diHE-dioxo	2-tBu-Ph
1-2270	ring 19	2-tBu-Ph
1-2271	ring 20	2-tBu-Ph
1-2272	ring 21	2-tBu-Ph
1-2273	dioxo	2-sBu-Ph
1-2274	4-HM-dioxo	2-sBu-Ph
1-2275	4,5-diHM-dioxo	2-sBu-Ph
1-2276	4,5-diHE-dioxo	2-sBu-Ph
1-2277	ring 19	2-sBu-Ph
1-2278	ring 20	2-sBu-Ph
1-2279	ring 21	2-sBu-Ph
1-2280	dioxo	2-OMe-Ph
1-2281	4-HM-dioxo	2-OMe-Ph
1-2282	4,5-diHM-dioxo	2-OMe-Ph
1-2283	4,5-diHE-dioxo	2-OMe-Ph
1-2284	ring 19	2-OMe-Ph
1-2285	ring 20	2-OMe-Ph
1-2286	ring 21	2-OMe-Ph
1-2287	dioxo	2-OEt-Ph
1-2288	4-HM-dioxo	2-OEt-Ph
1-2289	4,5-diHM-dioxo	2-OEt-Ph
1-2290	4,5-diHE-dioxo	2-OEt-Ph
1-2291	ring 19	2-OEt-Ph
1-2292	ring 20	2-OEt-Ph
1-2293	ring 21	2-OEt-Ph
1-2294	dioxo	2-$OCHF_2$-Ph
1-2295	4-HM-dioxo	2 $OCHF_2$-Ph
1-2296	4,5-diHM-dioxo	2-$OCHF_2$-Ph
1-2297	4,5-diHE-dioxo	2-$OCHF_2$-Ph
1-2298	ring 19	2-$OCHF_2$-Ph
1-2299	ring 20	2-$OCHF_2$-Ph
1-2300	ring 21	2-$OCHF_2$-Ph
1-2301	dioxo	2-SMe-Ph
1-2302	4-HM-dioxo	2-SMe-Ph
1-2303	4,5-diHM-dioxo	2-SMe-Ph
1-2304	4,5-diHE-dioxo	2-SMe-Ph
1-2305	ring 19	2-SMe-Ph
1-2306	ring 20	2-SMe-Ph
1-2307	ring 21	2-SMe-Ph
1-2308	dioxo	2-Ac-Ph
1-2309	4-HM-dioxo	2-Ac-Ph
1-2310	4,5-diHM-dioxo	2-Ac-Ph
1-2311	4,5-diHE-dioxo	2-Ac-Ph
1-2312	ring 19	2-Ac-Ph
1-2313	ring 20	2-Ac-Ph
1-2314	ring 21	2-Ac-Ph

TABLE 1-continued



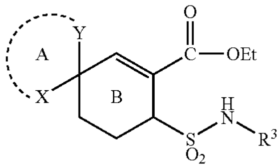
Compound No.	X, Y	R^3
1-2315	dioxo	2-Bn-Ph
1-2316	4-HM-dioxo	2-Bn-Ph
1-2317	4,5-diHM-dioxo	2-Bn-Ph
1-2318	4,5-diHE-dioxo	2-Bn-Ph
1-2319	ring 19	2-Bn-Ph
1-2320	ring 20	2-Bn-Ph
1-2321	ring 21	2-Bn-Ph
1-2322	dioxo	2-Mor-Ph
1-2323	4-HM-dioxo	2-Mor-Ph
1-2324	4,5-diHM-dioxo	2-Mor-Ph
1-2325	4,5-diHE-dioxo	2-Mor-Ph
1-2326	ring 19	2-Mor-Ph
1-2327	ring 20	2-Mor-Ph
1-2328	ring 21	2-Mor-Ph
1-2329	dioxo	Flu
1-2330	4-HM-dioxo	Flu
1-2331	4,5-diHM-dioxo	Flu
1-2332	4,5-diHE-dioxo	Flu
1-2333	ring 19	Flu
1-2334	ring 20	Flu
1-2335	ring 21	Flu
1-2336	dioxo	2-CH_2CH_2Pyrd-Ph
1-2337	4-HM-dioxo	2-CH_2CH_2Pyrd-Ph
1-2338	4,5-diHM-dioxo	2-CH_2CH_2Pyrd-Ph
1-2339	4,5-diHE-dioxo	2-CH_2CH_2Pyrd-Ph
1-2340	ring 19	2-CH_2CH_2Pyrd-Ph
1-2341	ring 20	2-CH_2CH_2Pyrd-Ph
1-2342	ring 21	2-CH_2CH_2Pyrd-Ph
1-2343	dioxo	2-CH_2CH_2NHBoc-Ph
1-2344	4-HM-dioxo	2-CH_2CH_2NHBoc-Ph
1-2345	4,5-diHM-dioxo	2-CH_2CH_2NHBoc-Ph
1-2346	4,5-diHE-dioxo	2-CH_2CH_2NHBoc-Ph
1-2347	ring 19	2-CH_2CH_2NHBoc-Ph
1-2348	ring 20	2-CH_2CH_2NHBoc-Ph
1-2349	ring 21	2-CH_2CH_2NHBoc-Ph
1-2350	dioxo	2-NH_2-Ph
1-2351	4-HM-dioxo	2-NH_2-Ph
1-2352	4,5-diHM-dioxo	2-NH_2-Ph
1-2353	4,5-diHE-dioxo	2-NH_2-Ph
1-2354	ring 19	2-NH_2-Ph
1-2355	ring 20	2-NH_2-Ph
1-2356	ring 21	2-NH_2-Ph
1-2357	dioxo	4-F-2-Me-Ph
1-2358	4-HM-dioxo	4-F-2-Me-Ph
1-2359	4,5-diHM-dioxo	4-F-2-Me-Ph
1-2360	4,5-diHE-dioxo	4-F-2-Me-Ph
1-2361	ring 19	4-F-2-Me-Ph
1-2362	ring 20	4-F-2-Me-Ph
1-2363	ring 21	4-F-2-Me-Ph
1-2364	dioxo	3-Cl-4-F-Ph
1-2365	4-HM-dioxo	3-Cl-4-F-Ph
1-2366	4,5-diHM-dioxo	3-Cl-4-F-Ph
1-2367	4,5-diHE-dioxo	3-Cl-4-F-Ph
1-2368	ring 19	3-Cl-4-F-Ph
1-2369	ring 20	3-Cl-4-F-Ph
1-2370	ring 21	3-Cl-4-F-Ph
1-2371	dioxo	4-F-3-CF_3-Ph
1-2372	4-HM-dioxo	4-F-3-CF_3-Ph
1-2373	4,5-diHM-dioxo	4-F-3-CF_3-Ph
1-2374	4,5-diHE-dioxo	4-F-3-CF_3-Ph
1-2375	ring 19	4-F-3-CF_3-Ph
1-2376	ring 20	4-F-3-CF_3-Ph
1-2377	ring 21	4-F-3-CF_3-Ph
1-2378	dioxo	4-F-3-OMe-Ph
1-2379	4-HM-dioxo	4-F-3-OMe-Ph
1-2380	4,5-diHM-dioxo	4-F-3-OMe-Ph
1-2381	4,5-diHE-dioxo	4-F-3-OMe-Ph
1-2382	ring 19	4-F-3-OMe-Ph

TABLE 1-continued



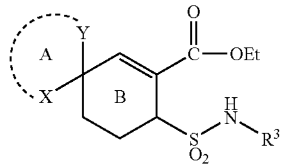
Compound No.	X, Y	R^3
1-2383	ring 20	4-F-3-OMe-Ph
1-2384	ring 21	4-F-3-OMe-Ph
1-2385	dioxo	3,4-diF-Ph
1-2386	4-HM-dioxo	3,4-diF-Ph
1-2387	4,5-diHM-dioxo	3,4-diF-Ph
1-2388	4,5-diHE-dioxo	3,4-diF-Ph
1-2389	ring 19	3,4-diF-Ph
1-2390	ring 20	3,4-diF-Ph
1-2391	ring 21	3,4-diF-Ph
1-2392	dioxo	2,4-diOMe-Ph
1-2393	4-HM-dioxo	2,4-diOMe-Ph
1-2394	4,5-diHM-dioxo	2,4-diOMe-Ph
1-2395	4,5-diHE-dioxo	2,4-diOMe-Ph
1-2396	ring 19	2,4-diOMe-Ph
1-2397	ring 20	2,4-diOMe-Ph
1-2398	ring 21	2,4-diOMe-Ph
1-2399	dioxo	4-Cl-2-F-Ph
1-2400	4-HM-dioxo	4-Cl-2-F-Ph
1-2401	4,5-diHM-dioxo	4-Cl-2-F-Ph
1-2402	4,5-diHE-dioxo	4-Cl-2-F-Ph
1-2403	ring 19	4-Cl-2-F-Ph
1-2404	ring 20	4-Cl-2-F-Ph
1-2405	ring 21	4-Cl-2-F-Ph
1-2406	dioxo	2-Br-4-Cl-Ph
1-2407	4-HM-dioxo	2-Br-4-Cl-Ph
1-2408	4,5-diHM-dioxo	2-Br-4-Cl-Ph
1-2409	4,5-diHE-dioxo	2-Br-4-Cl-Ph
1-2410	ring 19	2-Br-4-Cl-Ph
1-2411	ring 20	2-Br-4-Cl-Ph
1-2412	ring 21	2-Br-4-Cl-Ph
1-2413	dioxo	4-Cl-2-Me-Ph
1-2414	4-HM-dioxo	4-Cl-2-Me-Ph
1-2415	4,5-diHM-dioxo	4-Cl-2-Me-Ph
1-2416	4,5-diHE-dioxo	4-Cl-2-Me-Ph
1-2417	ring 19	4-Cl-2-Me-Ph
1-2418	ring 20	4-Cl-2-Me-Ph
1-2419	ring 21	4-Cl-2-Me-Ph
1-2420	dioxo	4-Cl-2-CO_2Me-Ph
1-2421	4-HM-dioxo	4-Cl-2-CO_2Me-Ph
1-2422	4,5-diHM-dioxo	4-Cl-2-CO_2Me-Ph
1-2423	4,5-diHE-dioxo	4-Cl-2-CO_2Me-Ph
1-2424	ring 19	4-Cl-2-CO_2Me-Ph
1-2425	ring 20	4-Cl-2-CO_2Me-Ph
1-2426	ring 21	4-Cl-2-CO_2Me-Ph
1-2427	dioxo	3,4-diCl-Ph
1-2428	4-HM-dioxo	3,4-diCl-Ph
1-2429	4,5-diHM-dioxo	3,4-diCl-Ph
1-2430	4,5-diHE-dioxo	3,4-diCl-Ph
1-2431	ring 19	3,4-diCl-Ph
1-2432	ring 20	3,4-diCl-Ph
1-2433	ring 21	3,4-diCl-Ph
1-2434	dioxo	2,5-diF-Ph
1-2435	4-HM-dioxo	2,5-diF-Ph
1-2436	4,5-diHM-dioxo	2,5-diF-Ph
1-2437	4,5-diHE-dioxo	2,5-diF-Ph
1-2438	ring 19	2,5-diF-Ph
1-2439	ring 20	2,5-diF-Ph
1-2440	ring 21	2,5-diF-Ph
1-2441	dioxo	2,6-diF-Ph
1-2442	4-HM-dioxo	2,6-diF-Ph
1-2443	4,5-diHM-dioxo	2,6-diF-Ph
1-2444	4,5-diHE-dioxo	2,6-diF-Ph
1-2445	ring 19	2,6-diF-Ph
1-2446	ring 20	2,6-diF-Ph
1-2447	ring 21	2,6-diF-Ph
1-2448	dioxo	2-F-4-Me-Ph
1-2449	4-HM-dioxo	2-F-4-Me-Ph
1-2450	4,5-diHM-dioxo	2-F-4-Me-Ph

TABLE 1-continued



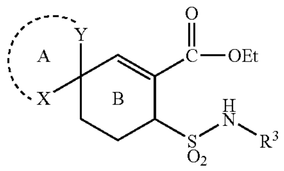
Compound No.	X, Y	R^3
1-2451	4,5-diHE-dioxo	2-F-4-Me-Ph
1-2452	ring 19	2-F-4-Me-Ph
1-2453	ring 20	2-F-4-Me-Ph
1-2454	ring 21	2-F-4-Me-Ph
1-2455	dioxo	2-F-5-Me-Ph
1-2456	4-HM-dioxo	2-F-5-Me-Ph
1-2457	4,5-diHM-dioxo	2-F-5-Me-Ph
1-2458	4,5-diHE-dioxo	2-F-5-Me-Ph
1-2459	ring 19	2-F-5-Me-Ph
1-2460	ring 20	2-F-5-Me-Ph
1-2461	ring 21	2-F-5-Me-Ph
1-2462	dioxo	2-F-4-OMe-Ph
1-2463	4-HM-dioxo	2-F-4-OMe-Ph
1-2464	4,5-diHM-dioxo	2-F-4-OMe-Ph
1-2465	4,5-diHE-dioxo	2-F-4-OMe-Ph
1-2466	ring 19	2-F-4-OMe-Ph
1-2467	ring 20	2-F-4-OMe-Ph
1-2468	ring 21	2-F-4-OMe-Ph
1-2469	dioxo	5-Cl-2-F-Ph
1-2470	4-HM-dioxo	5-Cl-2-F-Ph
1-2471	4,5-diHM-dioxo	5-Cl-2-F-Ph
1-2472	4,5-diHE-dioxo	5-Cl-2-F-Ph
1-2473	ring 19	5-Cl-2-F-Ph
1-2474	ring 20	5-Cl-2-F-Ph
1-2475	ring 21	5-Cl-2-F-Ph
1-2476	dioxo	2,3,4-triF-Ph
1-2477	4-HM-dioxo	2,3,4-triF-Ph
1-2478	4,5-diHM-dioxo	2,3,4-triF-Ph
1-2479	4,5-diHE-dioxo	2,3,4-triF-Ph
1-2480	ring 19	2,3,4-triF-Ph
1-2481	ring 20	2,3,4-triF-Ph
1-2482	ring 21	2,3,4-triF-Ph
1-2483	dioxo	2,4,5-triF-Ph
1-2484	4-HM-dioxo	2,4,5-triF-Ph
1-2485	4,5-diHM-dioxo	2,4,5-triF-Ph
1-2486	4,5-diHE-dioxo	2,4,5-triF-Ph
1-2487	ring 19	2,4,5-triF-Ph
1-2488	ring 20	2,4,5-triF-Ph
1-2489	ring 21	2,4,5-triF-Ph
1-2490	dioxo	2,4,6-triF-Ph
1-2491	4-HM-dioxo	2,4,6-triF-Ph
1-2492	4,5-diHM-dioxo	2,4,6-triF-Ph
1-2493	4,5-diHE-dioxo	2,4,6-triF-Ph
1-2494	ring 19	2,4,6-triF-Ph
1-2495	ring 20	2,4,6-triF-Ph
1-2496	ring 21	2,4,6-triF-Ph
1-2497	dioxo	2,4-diCl-Ph
1-2498	4-HM-dioxo	2,4-diCl-Ph
1-2499	4,5-diHM-dioxo	2,4-diCl-Ph
1-2500	4,5-diHE-dioxo	2,4-diCl-Ph
1-2501	ring 19	2,4-diCl-Ph
1-2502	ring 20	2,4-diCl-Ph
1-2503	ring 21	2,4-diCl-Ph
1-2504	dioxo	4-Br-2-Cl-Ph
1-2505	4-HM-dioxo	4-Br-2-Cl-Ph
1-2506	4,5-diHM-dioxo	4-Br-2-Cl-Ph
1-2507	4,5-diHE-dioxo	4-Br-2-Cl-Ph
1-2508	ring 19	4-Br-2-Cl-Ph
1-2509	ring 20	4-Br-2-Cl-Ph
1-2510	ring 21	4-Br-2-Cl-Ph
1-2511	dioxo	4-tBu-2-Cl-Ph
1-2512	4-HM-dioxo	4-tBu-2-Cl-Ph
1-2513	4,5-diHM-dioxo	4-tBu-2-Cl-Ph
1-2514	4,5-diHE-dioxo	4-tBu-2-Cl-Ph
1-2515	ring 19	4-tBu-2-Cl-Ph
1-2516	ring 20	4-tBu-2-Cl-Ph
1-2517	ring 21	4-tBu-2-Cl-Ph
1-2518	dioxo	2-Cl-6-F-Ph

TABLE 1-continued



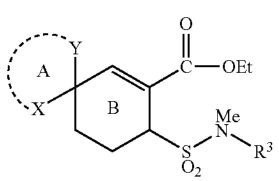
Compound No.	X, Y	R^3
1-2519	4-HM-dioxo	2-Cl-6-F-Ph
1-2520	4,5-diHM-dioxo	2-Cl-6-F-Ph
1-2521	4,5-diHE-dioxo	2-Cl-6-F-Ph
1-2522	ring 19	2-Cl-6-F-Ph
1-2523	ring 20	2-Cl-6-F-Ph
1-2524	ring 21	2-Cl-6-F-Ph
1-2525	dioxo	2,6-diCl-Ph
1-2526	4-HM-dioxo	2,6-diCl-Ph
1-2527	4,5-diHM-dioxo	2,6-diCl-Ph
1-2528	4,5-diHE-dioxo	2,6-diCl-Ph
1-2529	ring 19	2,6-diCl-Ph
1-2530	ring 20	2,6-diCl-Ph
1-2531	ring 21	2,6-diCl-Ph
1-2532	dioxo	2,3-diCl-Ph
1-2533	4-HM-dioxo	2,3-diCl-Ph
1-2534	4,5-diHM-dioxo	2,3-diCl-Ph
1-2535	4,5-diHE-dioxo	2,3-diCl-Ph
1-2536	ring 19	2,3-diCl-Ph
1-2537	ring 20	2,3-diCl-Ph
1-2538	ring 21	2,3-diCl-Ph
1-2539	dioxo	2,5-diCl-Ph
1-2540	4-HM-dioxo	2,5-diCl-Ph
1-2541	4,5-diHM-dioxo	2,5-diCl-Ph
1-2542	4,5-diHE-dioxo	2,5-diCl-Ph
1-2543	ring 19	2,5-diCl-Ph
1-2544	ring 20	2,5-diCl-Ph
1-2545	ring 21	2,5-diCl-Ph
1-2546	dioxo	2-Cl-4,6-diF-Ph
1-2547	4-HM-dioxo	2-Cl-4,6-diF-Ph
1-2548	4,5-diHM-dioxo	2-Cl-4,6-diF-Ph
1-2549	4,5-diHE-dioxo	2-Cl-4,6-diF-Ph
1-2550	ring 19	2-Cl-4,6-diF-Ph
1-2551	ring 20	2-Cl-4,6-diF-Ph
1-2552	ring 21	2-Cl-4,6-diF-Ph
1-2553	dioxo	2,6-diCl-4-F-Ph
1-2554	4-HM-dioxo	2,6-diCl-4-F-Ph
1-2555	4,5-diHM-dioxo	2,6-diCl-4-F-Ph
1-2556	4,5-diHE-dioxo	2,6-diCl-4-F-Ph
1-2557	ring 19	2,6-diCl-4-F-Ph
1-2558	ring 20	2,6-diCl-4-F-Ph
1-2559	ring 21	2,6-diCl-4-F-Ph
1-2560	dioxo	2-Br-6-Cl-4-F-Ph
1-2561	4-HM-dioxo	2-Br-6-Cl-4-F-Ph
1-2562	4,5-diHM-dioxo	2-Br-6-Cl-4-F-Ph
1-2563	4,5-diHE-dioxo	2-Br-6-Cl-4-F-Ph
1-2564	ring 19	2-Br-6-Cl-4-F-Ph
1-2565	ring 20	2-Br-6-Cl-4-F-Ph
1-2566	ring 21	2-Br-6-Cl-4-F-Ph
1-2567	dioxo	4-Cl-2-OMe-5-Me-Ph
1-2568	4-HM-dioxo	4-Cl-2-OMe-5-Me-Ph
1-2569	4,5-diHM-dioxo	4-Cl-2-OMe-5-Me-Ph
1-2570	4,5-diHE-dioxo	4-Cl-2-OMe-5-Me-Ph
1-2571	ring 19	4-Cl-2-OMe-5-Me-Ph
1-2572	ring 20	4-Cl-2-OMe-5-Me-Ph
1-2573	ring 21	4-Cl-2-OMe-5-Me-Ph
1-2574	dioxo	2,4-diBr-Ph
1-2575	4-HM-dioxo	2,4-diBr-Ph
1-2576	4,5-diHM-dioxo	2,4-diBr-Ph
1-2577	4,5-diHE-dioxo	2,4-diBr-Ph
1-2578	ring 19	2,4-diBr-Ph
1-2579	ring 20	2,4-diBr-Ph
1-2580	ring 21	2,4-diBr-Ph
1-2581	dioxo	2,6-diBr-Ph
1-2582	4-HM-dioxo	2,6-diBr-Ph
1-2583	4,5-diHM-dioxo	2,6-diBr-Ph
1-2584	4,5-diHE-dioxo	2,6-diBr-Ph
1-2585	ring 19	2,6-diBr-Ph
1-2586	ring 20	2,6-diBr-Ph

TABLE 1-continued



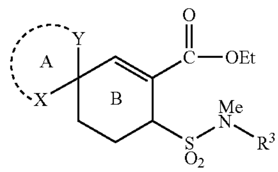
Compound No.	X, Y	R^3
1-2587	ring 21	2,6-diBr-Ph
1-2588	dioxo	2-Br-4-iPr-Ph
1-2589	4-HM-dioxo	2-Br-4-iPr-Ph
1-2590	4,5-diHM-dioxo	2-Br-4-iPr-Ph
1-2591	4,5-diHE-dioxo	2-Br-4-iPr-Ph
1-2592	ring 19	2-Br-4-iPr-Ph
1-2593	ring 20	2-Br-4-iPr-Ph
1-2594	ring 21	2-Br-4-iPr-Ph
1-2595	dioxo	2-nNon-Ph
1-2596	4-HM-dioxo	2-nNon-Ph
1-2597	4,5-diHM-dioxo	2-nNon-Ph
1-2598	4,5-diHE-dioxo	2-nNon-Ph
1-2599	ring 19	2-nNon-Ph
1-2600	ring 20	2-nNon-Ph
1-2601	ring 21	2-nNon-Ph
1-2602	dioxo	4-F-2-nNon-Ph
1-2603	4-HM-dioxo	4-F-2-nNon-Ph
1-2604	4,5-diHM-dioxo	4-F-2-nNon-Ph
1-2605	4,5-diHE-dioxo	4-F-2-nNon-Ph
1-2606	ring 19	4-F-2-nNon-Ph
1-2607	ring 20	4-F-2-nNon-Ph
1-2608	ring 21	4-F-2-nNon-Ph
1-2609	dioxo	2-nDec-Ph
1-2610	4-HM-dioxo	2-nDec-Ph
1-2611	4,5-diHM-dioxo	2-nDec-Ph
1-2612	4,5-diHE-dioxo	2-nDec-Ph
1-2613	ring 19	2-nDec-Ph
1-2614	ring 20	2-nDec-Ph
1-2615	ring 21	2-nDec-Ph
1-2616	dioxo	4-F-2-nDec-Ph
1-2617	4-HM-dioxo	4-F-2-nDec-Ph
1-2618	4,5-diHM-dioxo	4-F-2-nDec-Ph
1-2619	4,5-diHE-dioxo	4-F-2-nDec-Ph
1-2620	ring 19	4-F-2-nDec-Ph
1-2621	ring 20	4-F-2-nDec-Ph
1-2622	ring 21	4-F-2-nDec-Ph
1-2623	dioxo	2-Et-4-F-Ph
1-2624	4-HM-dioxo	2-Et-4-F-Ph
1-2625	4,5-diHM-dioxo	2-Et-4-F-Ph
1-2626	4,5-diHE-dioxo	2-Et-4-F-Ph
1-2627	ring 19	2-Et-4-F-Ph
1-2628	ring 20	2-Et-4-F-Ph
1-2629	ring 21	2-Et-4-F-Ph

TABLE 2



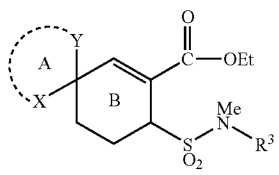
Compound No.	X, Y	R^3
2-1	dioxo	2-Cl-Ph
2-2	4-HM-dioxo	2-Cl-Ph
2-3	4,5-diHM-dioxo	2-Cl-Ph
2-4	4,5-diHE-dioxo	2-Cl-Ph
2-5	dioxo	2-Br-Ph
2-6	4-HM-dioxo	2-Br-Ph
2-7	4,5-diHM-dioxo	2-Br-Ph

TABLE 2-continued



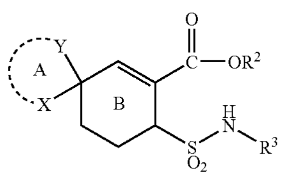
Compound No.	X, Y	R^3
2-8	4,5-diHE-dioxo	2-Br-Ph
2-9	dioxo	2-Cl-6-Me-Ph
2-10	4-HM-dioxo	2-Cl-6-Me-Ph
2-11	4,5-diHM-dioxo	2-Cl-6-Me-Ph
2-12	4,5-diHE-dioxo	2-Cl-6-Me-Ph
2-13	dioxo	2-Cl-4-F-Ph
2-14	4-HM-dioxo	2-Cl-4-F-Ph
2-15	4,5-diHM-dioxo	2-Cl-4-F-Ph
2-16	4,5-diHE-dioxo	2-Cl-4-F-Ph
2-17	dioxo	2,4-diF
2-18	4-HM-dioxo	2,4-diF
2-19	4,5-diHM-dioxo	2,4-diF
2-20	4,5-diHE-dioxo	2,4-diF
2-21	dioxo	2-Br-4-F-Ph
2-22	4-HM-dioxo	2-Br-4-F-Ph
2-23	4,5-diHM-dioxo	2-Br-4-F-Ph
2-24	4,5-diHE-dioxo	2-Br-4-F-Ph
2-25	dioxo	2-nBu-4-F-Ph
2-26	4-HM-dioxo	2-nBu-4-F-Ph
2-27	4,5-diHM-dioxo	2-nBu-4-F-Ph
2-28	4,5-diHE-dioxo	2-nBu-4-F-Ph
2-29	dioxo	2-nPent-Ph
2-30	4-HM-dioxo	2-nPent-Ph
2-31	4,5-diHM-dioxo	2-nPent-Ph
2-32	4,5-diHE-dioxo	2-nPent-Ph
2-33	dioxo	4-F-2-nPent-Ph
2-34	4-HM-dioxo	4-F-2-nPent-Ph
2-35	4,5-diHM-dioxo	4-F-2-npent-Ph
2-35	4,5-diHE-dioxo	4-F-2-nPent-Ph
2-37	dioxo	2-nHex-Ph
2-38	4-HM-dioxo	2-nHex-Ph
2-39	4,5-diHM-dioxo	2-nHex-Ph
2-40	4,5-diHE-dioxo	2-nHex-Ph
2-41	dioxo	4-F-2-nHex-Ph
2-42	4-HM-dioxo	4-F-2-nHex-Ph
2-43	4,5-diHM-dioxo	4-F-2-nHex-Ph
2-44	4,5-diHE-dioxo	4-F-2-nHex-Ph
2-45	dioxo	2-nHept-Ph
2-46	4-HM-dioxo	2-nHept-Ph
2-47	4,5-diHM-dioxo	2-nHept-Ph
2-48	4,5-diHE-dioxo	2-nHept-Ph
2-49	dioxo	4-F-2-nHept-Ph
2-50	4-HM-dioxo	4-F-2-nHept-Ph
2-51	4,5-diHM-dioxo	4-F-2-nHept-Ph
2-52	4,5-diHE-dioxo	4-F-2-nHept-Ph
2-53	dioxo	2-nOct-Ph
2-54	4-HM-dioxo	2-nOct-Ph
2-55	4,5-diHM-dioxo	2-nOct-Ph
2-56	4,5-diHE-dioxo	2-nOct-Ph
2-57	dioxo	4-F-2-nOct-Ph
2-58	4-HM-dioxo	4-F-2-nOct-Ph
2-59	4,5-diHM-dioxo	4-F-2-nOct-Ph
2-60	4,5-diHE-dioxo	4-F-2-nOct-Ph
2-61	dioxo	Ph
2-62	4-HM-dioxo	Ph
2-63	4,5-diHM-dioxo	Ph
2-64	4,5-diHE-dioxo	Ph
2-65	dioxo	4-F-Ph
2-66	4-HM-dioxo	4-F-Ph
2-67	4,5-diHM-dioxo	4-F-Ph
2-68	4,5-diHE-dioxo	4-F-Ph
2-69	dioxo	2-C1-4-Me-Ph
2-70	4-HM-dioxo	2-C1-4-Me-Ph
2-71	4,5-diHM-dioxo	2-C1-4-Me-Ph
2-72	4,5-diHE-dioxo	2-C1-4-Me-Ph
2-73	dioxo	2-nBu-Ph
2-74	4-HM-dioxo	2-nBu-Ph

TABLE 2-continued



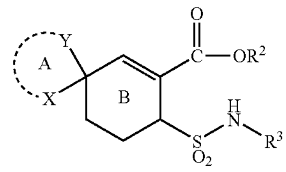
Compound No.	X, Y	R^3
2-75	4,5-diHM-dioxo	2-nBu-Ph
2-76	4,5-diHE-dioxo	2-nBu-Ph
2-77	dioxo	2-nPr-Ph
2-78	4-HM-dioxo	2-nPr-Ph
2-79	4,5-diHM-dioxo	2-nPr-Ph
2-80	4,5-diHE-dioxo	2-nPr-Ph
2-81	dioxo	4-F-2-nPr-Ph
2-82	4-HM-dioxo	4-F-2-nPr-Ph
2-83	4,5-diHM-dioxo	4-F-2-nPr-Ph
2-84	4,5-diHE-dioxo	4-F-2-nPr-Ph

TABLE 3



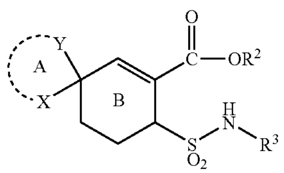
Compound No.	X, Y	R^2	R^3
3-1	dioxo	Me	2-Cl-Ph
3-2	4-HM-dioxo	Me	2-Cl-Ph
3-3	4,5-diHM-dioxo	Me	2-Cl-Ph
3-4	4,5-diHE-dioxo	Me	2-Cl-Ph
3-5	dioxo	nPr	2-Cl-Ph
3-6	4-HM-dioxo	nPr	2-Cl-Ph
3-7	4,5-diHM-dioxo	nPr	2-Cl-Ph
3-8	4,5-diHE-dioxo	nPr	2-Cl-Ph
3-9	dioxo	nBu	2-Cl-Ph
3-10	4-HM-dioxo	nBu	2-Cl-Ph
3-11	4,5-diHM-dioxo	nBu	2-Cl-Ph
3-12	4,5-diHE-dioxo	nBu	2-Cl-Ph
3-13	dioxo	iPr	2-Cl-Ph
3-14	4-HM-dioxo	iPr	2-Cl-Ph
3-15	4,5-diHM-dioxo	iPr	2-Cl-Ph
3-16	4,5-diHE-dioxo	iPr	2-Cl-Ph
3-17	dioxo	tBu	2-Cl-Ph
3-18	4-HM-dioxo	tBu	2-Cl-Ph
3-19	4,5-diHM-dioxo	tBu	2-Cl-Ph
3-20	4,5-diHE-dioxo	tBu	2-Cl-Ph
3-21	dioxo	CH_2OAc	2-Cl-Ph
3-22	4-HM-dioxo	CH_2OAc	2-Cl-Ph
3-23	4,5-diHM-dioxo	CH_2OAc	2-Cl-Ph
3-24	4,5-diHE-dioxo	CH_2OAc	2-Cl-Ph
3-25	dioxo	Me	2-Br-Ph
3-26	4-HM-dioxo	Me	2-Br-Ph
3-27	4,5-diHM-dioxo	Me	2-Br-Ph
3-28	4,5-diHE-dioxo	Me	2-Br-Ph
3-29	dioxo	nPr	2-Br-Ph
3-30	4-HM-dioxo	nPr	2-Br-Ph
3-31	4,5-diHM-dioxo	nPr	2-Br-Ph
3-32	4,5-diHE-dioxo	nPr	2-Br-Ph
3-33	dioxo	nBu	2-Br-Ph
3-34	4-HM-dioxo	nBu	2-Br-Ph
3-35	4,5-diHM-dioxo	nBu	2-Br-Ph
3-36	4,5-diHE-dioxo	nBu	2-Br-Ph
3-37	dioxo	iPr	2-Br-Ph
3-38	4-HM-dioxo	iPr	2-Br-Ph
3-39	4,5-diHM-dioxo	iPr	2-Br-Ph

TABLE 3-continued



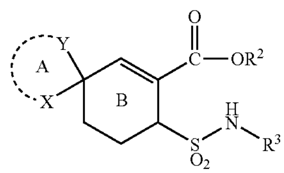
Compound No.	X, Y	R^2	R^3
3-40	4,5-diHE-dioxo	iPr	2-Br-Ph
3-41	dioxo	tBu	2-Br-Ph
3-42	4-HM-dioxo	tBu	2-Br-Ph
3-43	4,5-diHM-dioxo	tBu	2-Br-Ph
3-44	4,5-diHE-dioxo	tBu	2-Br-Ph
3-45	dioxo	CH_2OAc	2-Br-Ph
3-45	4-HM-dioxo	CH_2OAc	2-Br-Ph
3-47	4,5-diHM-dioxo	CH_2OAc	2-Br-Ph
3-48	4,5-diHE-dioxo	CH_2OAc	2-Br-Ph
3-49	dioxo	Me	2-Cl-6-Me-Ph
3-50	4-HM-dioxo	Me	2-Cl-6-Me-Ph
3-51	4,5-diHM-dioxo	Me	2-Cl-6-Me-Ph
3-52	4,5-diHE-dioxo	Me	2-Cl-6-Me-Ph
3-53	dioxo	nPr	2-Cl-6-Me-Ph
3-54	4-HM-dioxo	nPr	2-Cl-6-Me-Ph
3-55	4,5-diHM-dioxo	nPr	2-Cl-6-Me-Ph
3-56	4,5-diHE-dioxo	nPr	2-Cl-6-Me-Ph
3-57	dioxo	nBu	2-Cl-6-Me-Ph
3-58	4-HM-dioxo	nBu	2-Cl-6-Me-Ph
3-59	4,5-diHM-dioxo	nBu	2-Cl-6-Me-Ph
3-60	4,5-diHE-dioxo	nBu	2-Cl-6-Me-Ph
3-61	dioxo	iPr	2-Cl-6-Me-Ph
3-62	4-HM-dioxo	iPr	2-Cl-6-Me-Ph
3-63	4,5-diHM-dioxo	iPr	2-Cl-6-Me-Ph
3-64	4,5-diHE-dioxo	iPr	2-Cl-6-Me-Ph
3-65	dioxo	tBu	2-Cl-6-Me-Ph
3-66	4-HM-dioxo	tBu	2-Cl-6-Me-Ph
3-67	4,5-diHM-dioxo	tBu	2-Cl-6-Me-Ph
3-68	4,5-diHE-dioxo	tBu	2-Cl-6-Me-Ph
3-69	dioxo	CH_2OAc	2-Cl-6-Me-Ph
3-70	4-HM-dioxo	CH_2OAc	2-Cl-6-Me-Ph
3-71	4,5-diHM-dioxo	CH_2OAc	2-Cl-6-Me-Ph
3-72	4,5-diHE-dioxo	CH_2OAc	2-Cl-6-Me-Ph
3-73	dioxo	Me	2-Cl-4-F-Ph
3-74	4-HM-dioxo	Me	2-Cl-4-F-Ph
3-75	4,5-diHM-dioxo	Me	2-Cl-4-F-Ph
3-76	4,5-diHE-dioxo	Me	2-Cl-4-F-Ph
3-77	dioxo	nPr	2-Cl-4-F-Ph
3-78	4-HM-dioxo	nPr	2-Cl-4-F-Ph
3-79	4,5-diHM-dioxo	nPr	2-Cl-4-F-Ph
3-80	4,5-diHE-dioxo	nPr	2-Cl-4-F-Ph
3-81	dioxo	nBu	2-Cl-4-F-Ph
3-82	4-HM-dioxo	nBu	2-Cl-4-F-Ph
3-83	4,5-diHM-dioxo	nBu	2-Cl-4-F-Ph
3-84	4,5-diHE-dioxo	nBu	2-Cl-4-F-Ph
3-85	dioxo	iPr	2-Cl-4-F-Ph
3-86	4-HM-dioxo	iPr	2-Cl-4-F-Ph
3-87	4,5-diHM-dioxo	iPr	2-Cl-4-F-Ph
3-88	4,5-diHE-dioxo	iPr	2-Cl-4-F-Ph
3-89	dioxo	tBu	2-Cl-4-F-Ph
3-90	4-HM-dioxo	tBu	2-Cl-4-F-Ph
3-91	4,5-diHM-dioxo	tBu	2-Cl-4-F-Ph
3-92	4,5-diHE-dioxo	tBu	2-Cl-4-F-Ph
3-93	dioxo	CH_2OAc	2-Cl-4-F-Ph
3-94	4-HM-dioxo	CH_2OAc	2-Cl-4-F-Ph
3-95	4,5-diHM-dioxo	CH_2OAc	2-Cl-4-F-Ph
3-96	4,5-diHE-dioxo	CH_2OAc	2-Cl-4-F-Ph
3-97	dioxo	Me	2,4-diF-Ph
3-98	4-HM-dioxo	Me	2,4-diF-Ph
3-99	4,5-diHM-dioxo	Me	2,4-diF-Ph
3-100	4,5-diHE-dioxo	Me	2,4-diF-Ph
3-101	dioxo	nPr	2,4-diF-Ph
3-102	4-HM-dioxo	nPr	2,4-diF-Ph
3-103	4,5-diHM-dioxo	nPr	2,4-diF-Ph
3-104	4,5-diHE-dioxo	nPr	2,4-diF-Ph
3-105	dioxo	nBu	2,4-diF-Ph
3-106	4-HM-dioxo	nBu	2,4-diF-Ph

TABLE 3-continued



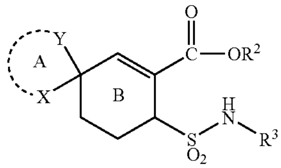
Compound No.	X, Y	R^2	R^3
3-107	4,5-diHM-dioxo	nBu	2,4-diF-Ph
3-108	4,5-diHE-dioxo	nBu	2,4-diF-Ph
3-109	dioxo	iPr	2,4-diF-Ph
3-110	4-HM-dioxo	iPr	2,4-diF-Ph
3-111	4,5-diHM-dioxo	iPr	2,4-diF-Ph
3-112	4,5-diHE-dioxo	iPr	2,4-diF-Ph
3-113	dioxo	tBu	2,4-diF-Ph
3-114	4-HM-dioxo	tBu	2,4-diF-Ph
3-115	4,5-diHM-dioxo	tBu	2,4-diF-Ph
3-116	4,5-diHE-dioxo	tBu	2,4-diF-Ph
3-117	dioxo	CH_2OAc	2,4-diF-Ph
3-118	4-HM-dioxo	CH_2OAc	2,4-diF-Ph
3-119	4,5-diHM-dioxo	CH_2OAc	2,4-diF-Ph
3-120	4,5-diHE-dioxo	CH_2OAc	2,4-diF-Ph
3-121	dioxo	Me	2-Br-4-F-Ph
3-122	4-HM-dioxo	Me	2-Br-4-F-Ph
3-123	4,5-diHM-dioxo	Me	2-Br-4-F-Ph
3-124	4,5-diHE-dioxo	Me	2-Br-4-F-Ph
3-125	dioxo	nPr	2-Br-4-F-Ph
3-126	4-HM-dioxo	nPr	2-Br-4-F-Ph
3-127	4,5-diHM-dioxo	nPr	2-Br-4-F-Ph
3-128	4,5-diHE-dioxo	nPr	2-Br-4-F-Ph
3-129	dioxo	nBu	2-Br-4-F-Ph
3-130	4-HM-dioxo	nBu	2-Br-4-F-Ph
3-131	4,5-diHM-dioxo	nBu	2-Br-4-F-Ph
3-132	4,5-diHE-dioxo	nBu	2-Br-4-F-Ph
3-133	dioxo	iPr	2-Br-4-F-Ph
3-134	4-HM-dioxo	iPr	2-Br-4-F-Ph
3-135	4,5-diHM-dioxo	iPr	2-Br-4-F-Ph
3-136	4,5-diHE-dioxo	iPr	2-Br-4-F-Ph
3-137	dioxo	tBu	2-Br-4-F-Ph
3-138	4-HM-dioxo	tBu	2-Br-4-F-Ph
3-139	4,5-diHM-dioxo	tBu	2-Br-4-F-Ph
3-140	4,5-diHE-dioxo	tBu	2-Br-4-F-Ph
3-141	dioxo	CH_2OAc	2-Br-4-F-Ph
3-142	4-HM-dioxo	CH_2OAc	2-Br-4-F-Ph
3-143	4,5-diHM-dioxo	CH_2OAc	2-Br-4-F-Ph
3-144	4,5-diHE-dioxo	CH_2OAc	2-Br-4-F-Ph
3-145	dioxo	Me	2-nBu-4-F-Ph
3-146	4-HM-dioxo	Me	2-nBu-4-F-Ph
3-147	4,5-diHM-dioxo	Me	2-nBu-4-F-Ph
3-148	4,5-diHE-dioxo	Me	2-nBu-4-F-Ph
3-149	dioxo	nPr	2-nBu-4-F-Ph
3-150	4-HM-dioxo	nPr	2-nBu-4-F-Ph
3-151	4,5-diHM-dioxo	nPr	2-nBu-4-F-Ph
3-152	4,5-diHE-dioxo	nPr	2-nBu-4-F-Ph
3-153	dioxo	nBu	2-nBu-4-F-Ph
3-154	4-HM-dioxo	nBu	2-nBu-4-F-Ph
3-155	4,5-diHM-dioxo	nBu	2-nBu-4-F-Ph
3-156	4,5-diHE-dioxo	nBu	2-nBu-4-F-Ph
3-157	dioxo	iPr	2-nBu-4-F-Ph
3-158	4-HM-dioxo	iPr	2-nBu-4-F-Ph
3-159	4,5-diHM-dioxo	iPr	2-nBu-4-F-Ph
3-160	4,5-diHE-dioxo	iPr	2-nBu-4-F-Ph
3-161	dioxo	tBu	2-nBu-4-F-Ph
3-162	4-HM-dioxo	tBu	2-nBu-4-F-Ph
3-163	4,5-diHM-dioxo	tBu	2-nBu-4-F-Ph
3-164	4,5-diHE-dioxo	tBu	2-nBu-4-F-Ph
3-165	dioxo	CH_2OAc	2-nBu-4-F-Ph
3-166	4-HM-dioxo	CH_2OAo	2-nBu-4-F-Ph
3-167	4,5-diHM-dioxo	CH_2OAc	2-nBu-4-F-Ph
3-168	4,5-diHE-dioxo	CH_2OAc	2-nBu-4-F-Ph
3-169	dioxo	Me	2-nPent-Ph
3-170	4-HM-dioxo	Me	2-nPent-Ph
3-171	4,5-diHM-dioxo	Me	2-nPent-Ph
3-172	4,5-diHE-dioxo	Me	2-nPent-Ph
3-173	dioxo	nPr	2-nPent-Ph

TABLE 3-continued



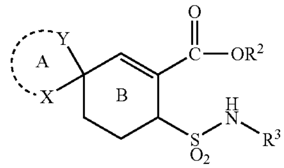
Compound No.	X, Y	R^2	R^3
3-174	4-HM-dioxo	nPr	2-nPent-Ph
3-175	4,5-diHM-dioxo	nPr	2-nPent-Ph
3-176	4,5-diHE-dioxo	nPr	2-nPent-Ph
3-177	dioxo	nBu	2-nPent-Ph
3-178	4-HM-dioxo	nBu	2-nPent-Ph
3-179	4,5-diHM-dioxo	nBu	2-nPent-Ph
3-180	4,5-diHE-dioxo	nBu	2-nPent-Ph
3-181	dioxo	iPr	2-nPent-Ph
3-182	4-HM-dioxo	iPr	2-nPent-Ph
3-183	4,5-diHM-dioxo	iPr	2-nPent-Ph
3-184	4,5-diHE-dioxo	iPr	2-nPent-Ph
3-185	dioxo	tBu	2-nPent-Ph
3-186	4-HM-dioxo	tBu	2-nPent-Ph
3-187	4,5-diHM-dioxo	tBu	2-nPent-Ph
3-188	4,5-diHE-dioxo	tBu	2-nPent-Ph
3-189	dioxo	CH_2OAc	2-nPent-Ph
3-190	4-HM-dioxo	CH_2OAc	2-nPent-Ph
3-191	4,5-diHM-dioxo	CH_2OAc	2-nPent-Ph
3-192	4,5-diHE-dioxo	CH_2OAc	2-nPent-Ph
3-193	dioxo	Me	4-F-2-nPent-Ph
3-194	4-HM-dioxo	Me	4-F-2-nPent-Ph
3-195	4,5-diHM-dioxo	Me	4-F-2-npent-Ph
3-196	4,5-diHE-dioxo	Me	4-F-2-npent-Ph
3-197	dioxo	nPr	4-F-2-nPent-Ph
3-198	4-HM-dioxo	nPr	4-F-2-nPent-Ph
3-199	4,5-diHM-dioxo	nPr	4-F-2-nPent-Ph
3-200	4,5-diHE-dioxo	nPr	4-F-2-nPent-Ph
3-201	dioxo	nBu	4-F-2-nPent-Ph
3-202	4-HM-dioxo	nBu	4-F-2-nPent-Ph
3-203	4,5-diHM-dioxo	nBu	4-F-2-nPent-Ph
3-204	4,5-diHE-dioxo	nBu	4-F-2-nPent-Ph
3-205	dioxo	iPr	4-F-2-nPent-Ph
3-206	4-HM-dioxo	iPr	4-F-2-nPent-Ph
3-207	4,5-diHM-dioxo	iPr	4-F-2-nPent-Ph
3-208	4,5-diHE-dioxo	iPr	4-F-2-nPent-Ph
3-209	dioxo	tBu	4-F-2-nPent-Ph
3-210	4-HM-dioxo	tBu	4-F-2-nPent-Ph
3-211	4,5-diHM-dioxo	tBu	4-F-2-nPent-Ph
3-212	4,5-diHE-dioxo	tBu	4-F-2-nPent-Ph
3-213	dioxo	CH_2OAc	4-F-2-nPent-Ph
3-214	4-HM-dioxo	CH_2OAc	4-F-2-nPent-Ph
3-215	4,5-diHM-dioxo	CH_2OAo	4-F-2-nPent-Ph
3-216	4,5-diHE-dioxo	CH_2OAo	4-F-2-nPent-Ph
3-217	dioxo	Me	2-nHex-Ph
3-218	4-HM-dioxo	Me	2-nHex-Ph
3-219	4,5-diHM-dioxo	Me	2-nHex-Ph
3-220	4,5-diHE-dioxo	Me	2-nHex-Ph
3-221	dioxo	nPr	2-nHex-Ph
3-222	4-HM-dioxo	nPr	2-nHex-Ph
3-223	4,5-diHM-dioxo	nPr	2-nHex-Ph
3-224	4,5-diHE-dioxo	nPr	2-nHex-Ph
3-225	dioxo	nBu	2-nHex-Ph
3-226	4-HM-dioxo	nBu	2-nHex-Ph
3-227	4,5-diHM-dioxo	nBu	2-nHex-Ph
3-223	4,5-diHE-dioxo	nBu	2-nHex-Ph
3-229	dioxo	iPr	2-nHex-Ph
3-230	4-HM-dioxo	iPr	2-nHex-Ph
3-231	4,5-diHM-dioxo	iPr	2-nHex-Ph
3-232	4,5-diHE-dioxo	iPr	2-nHex-Ph
3-233	dioxo	tBu	2-nHex-Ph
3-234	4-HM-dioxo	tBu	2-nHex-Ph
3-235	4,5-diHM-dioxo	tBu	2-nHex-Ph
3-236	4,5-diHE-dioxo	tBu	2-nHex-Ph
3-237	dioxo	CH_2OAc	2-nHex-Ph
3-238	4-HM-dioxo	CH_2OAc	2-nHex-Ph
3-239	4,5-diHM-dioxo	CH_2OAc	2-nHex-Ph
3-240	4,5-diHE-dioxo	CH_2OAc	2-nHex-Ph

TABLE 3-continued



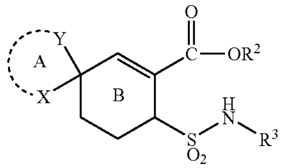
Compound No.	X, Y	R^2	R^3
3-241	dioxo	Me	4-F-nHex-Ph
3-242	4-HM-dioxo	Me	4-F-nHex-Ph
3-243	4,5-diHM-dioxo	Me	4-F-nHex-Ph
3-244	4,5-diHE-dioxo	Me	4-F-nHex-Ph
3-245	dioxo	nPr	4-F-nHex-Ph
3-246	4-HM-dioxo	nPr	4-F-nHex-Ph
3-247	4,5-diHM-dioxo	nPr	4-F-nHex-Ph
3-248	4,5-diHE-dioxo	nPr	4-F-nHex-Ph
3-249	dioxo	nBu	4-F-nHex-Ph
3-250	4-HM-dioxo	nBu	4-F-nHex-Ph
3-251	4,5-diHM-dioxo	nBu	4-F-nHex-Ph
3-252	4,5-diHE-dioxo	nBu	4-F-nHex-Ph
3-253	dioxo	iPr	4-F-nHex-Ph
3-254	4-HM-dioxo	iPr	4-F-nHex-Ph
3-255	4,5-diHM-dioxo	iPr	4-F-nHex-Ph
3-256	4,5-diHE-dioxo	iPr	4-F-nHex-Ph
3-257	dioxo	tBu	4-F-nHex-Ph
3-258	4-HM-dioxo	tBu	4-F-nHex-Ph
3-259	4,5-diHM-dioxa	tBu	4-F-nHex-Ph
3-260	4,5-diHE-dioxo	tBu	4-F-nHex-Ph
3-261	dioxo	CH_2OAc	4-F-nHex-Ph
3-262	4-HM-dioxo	CH_2OAc	4-F-nHex-Ph
3-263	4,5-diHM-dioxo	CH_2OAc	4-F-nHex-Ph
3-264	4,5-diHE-dioxo	CH_2OAC	4-F-nHex-Ph
3-265	dioxo	Me	2-nHept-Ph
3-266	4-HM-dioxo	Me	2-nHept-Ph
3-267	4,5-diHM-dioxo	Me	2-nHept-Ph
3-268	4,5-diHE-dioxo	Me	2-nHept-Ph
3-269	dioxo	nPr	2-nHept-Ph
3-270	4-HM-dioxo	nPr	2-nHept-Ph
3-271	4,5-diHM-dioxo	nPr	2-nHept-Ph
3-272	4,5-diHE-dioxo	nPr	2-nHept-Ph
3-273	dioxo	nBu	2-nHept-Ph
3-274	4-HM-dioxo	nBu	2-nHept-Ph
3-275	4,5-diHM-dioxo	nBu	2-nHept-Ph
3-276	4,5-diHE-dioxo	nBu	2-nHept-Ph
3-277	dioxo	iPr	2-nHept-Ph
3-278	4-HM-dioxo	iPr	2-nHept-Ph
3-279	4,5-diHM-dioxo	iPr	2-nHept-Ph
3-280	4,5-diHE-dioxo	iPr	2-nHept-Ph
3-281	dioxo	tBu	2-nHept-Ph
3-282	4-HM-dioxo	tBu	2-nHept-Ph
3-283	4,5-diHM-dioxo	tBu	2-nHept-Ph
3-284	4,5-diHE-dioxo	tBu	2-nHept-Ph
3-285	dioxo	CH_2OAc	2-nHept-Ph
3-286	4-HM-dioxo	CH_2OAc	2-nHept-Ph
3-287	4,5-diHM-dioxo	CH_2OAc	2-nHept-Ph
3-288	4,5-diHE-dioxo	CH_2OAc	2-nHept-Ph
3-289	dioxo	Me	4-F-2-nHept-Ph
3-290	4-HM-dioxo	Me	4-F-2-nHept-Ph
3-291	4,5-diHM-dioxo	Me	4-F-2-nHept-Ph
3-292	4,5-diHE-dioxo	Me	4-F-2-nHept-Ph
3-293	dioxo	nPr	4-F-2-nHept-Ph
3-294	4-HM-dioxo	nPr	4-F-2-nHept-Ph
3-295	4,5-diHM-dioxo	nPr	4-F-2-nHept-Ph
3-296	4,5-diHE-dioxo	nPr	4-F-2-nHept-Ph
3-297	dioxo	nBu	4-F-2-nHept-Ph
3-298	4-HM-dioxo	nBu	4-F-2-nHept-Ph
3-299	4,5-diHM-dioxo	nBu	4-F-2-nHept-Ph
3-300	4,5-diHE-dioxo	nBu	4-F-2-nHept-Ph
3-301	dioxo	iPr	4-F-2-nHept-Ph
3-302	4-HM-dioxo	iPr	4-F-2-nHept-Ph
3-303	4,5-diHM-dioxo	iPr	4-F-2-nHept-Ph
3-304	4,5-diHE-dioxo	iPr	4-F-2-nHept-Ph
3-305	dioxo	tBu	4-F-2-nHept-Ph
3-306	4-HM-dioxo	tBu	4-F-2-nHept-Ph
3-307	4,5-diHM-dioxo	tBu	4-F-2-nHept-Ph

TABLE 3-continued



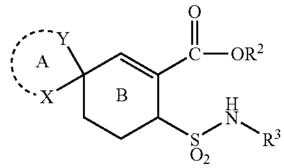
Compound No.	X, Y	R^2	R^3
3-308	4,5-diHE-dioxo	tBu	4-F-2-nHept-Ph
3-309	dioxo	CH_2OAc	4-F-2-nHept-Ph
3-310	4-HM-dioxo	CH_2OAc	4-F-2-nHept-Ph
3-311	4,5-diHM-dioxo	CH_2OAc	4-F-2-nHept-Ph
3-312	4,5-diHE-dioxo	CH_2OAc	4-F-2-nHept-Ph
3-313	dioxo	Me	2-nOct-Ph
3-314	4-HM-dioxo	Me	2-nOct-Ph
3-315	4,5-diHM-dioxo	Me	2-nOct-Ph
3-316	4,5-diHE-dioxo	Me	2-nOct-Ph
3-317	dioxo	nPr	2-nOct-Ph
3-318	4-HM-dioxo	nPr	2-nOct-Ph
3-319	4,5-diHM-dioxo	nPr	2-nOct-Ph
3-320	4,5-diHE--dioxo	nPr	2-nOct-Ph
3-321	dioxo	nBu	2-nOct-Ph
3-322	4-HM-dioxo	nBu	2-nOct-Ph
3-323	4,5-diHM-dioxo	nBu	2-nOct-Ph
3-324	4,5-diHE-dioxo	nBu	2-nOct-Ph
3-325	dioxo	iPr	2-nOct-Ph
3-326	4-HM-dioxo	iPr	2-nOct-Ph
3-327	4,5-diHM-dioxo	iPr	2-nOct-Ph
3-328	4,5-diHE-dioxo	iPr	2-nOct-Ph
3-329	dioxo	tBu	2-nOct-Ph
3-330	4-HM-dioxo	tBu	2-nOct-Ph
3-331	4,5-diHM-dioxo	tBu	2-nOct-Ph
3-332	4,5-diHE-dioxo	tBu	2-nOct-Ph
3-333	dioxo	CH_2OAo	2-nOct-Ph
3-334	4-HM-dioxo	CH_2OAc	2-nOct-Ph
3-335	4,5-diHM-dioxo	CH_2OAc	2-nOct-Ph
3-336	4,5-diHE-dioxo	CH_2OAc	2-nOct-Ph
3-337	dioxo	Me	4-F-2-nOct-Ph
3-338	4-HM-dioxo	Me	4-F-2-nOct-Ph
3-339	4,5-diHM-dioxo	Me	4-F-2-nOct-Ph
3-340	4,5-diHE-dioxo	Me	4-F-2-nOct-Ph
3-341	dioxo	nPr	4-F-2-nOct-Ph
3-342	4-HM-dioxo	nPr	4-F-2-nOct-Ph
3-343	4,5-diHM-dioxo	nPr	4-F-2-nOct-Ph
3-344	4,5-diHE-dioxo	nPr	4-F-2-nOct-Ph
3-345	dioxo	nBu	4-F-2-nOct-Ph
3-346	4-HM-dioxo	nBu	4-F-2-nOct-Ph
3-347	4,5-diHM-dioxo	nBu	4-F-2-nOct-Ph
3-348	4,5-diHE-dioxo	nBu	4-F-2-nOct-Ph
3-349	dioxo	iPr	4-F-2-nOct-Ph
3-350	4-HM-dioxo	iPr	4-F-2-nOct-Ph
3-351	4,5-diHM-dioxo	iPr	4-F-2-nOct-Ph
3-352	4,5-diHE-dioxo	iPr	4-F-2-nOct-Ph
3-353	dioxo	tBu	4-F-2-nOct-Ph
3-354	4-HM-dioxo	tBu	4-F-2-nOct-Ph
3-355	4,5-diHM-dioxo	tBu	4-F-2-nOct-Ph
3-356	4,5-diHE-dioxo	tBu	4-F-2-nOct-Ph
3-357	dioxo	CH_2OAc	4-F-2-nOct-Ph
3-358	4-HM-dioxo	CH_2OAc	4-F-2-nOct-Ph
3-359	4,5-diHM-dioxo	CH_2OAc	4-F-2-nOct-Ph
3-360	4,5-diHE-dioxo	CH_2OAc	4-F-2-nOct-Ph
3-361	dioxo	Me	Ph
3-362	4-HM-dioxo	Me	Ph
3-363	4,5-diHM-dioxo	Me	Ph
3-364	4,5-diHE-dioxo	Me	Ph
3-365	dioxo	nPr	Ph
3-366	4-HM-dioxo	nPr	Ph
3-367	4,5-diHM-dioxo	nPr	Ph
3-368	4,5-diHE-dioxo	nPr	Ph
3-369	dioxo	nBu	Ph
3-370	4-HM-dioxo	nBu	Ph
3-371	4,5-diHM-dioxo	nBu	Ph
3-372	4,5-diHE-dioxo	nBu	Ph
3-373	dioxo	iPr	Ph
3-374	4-HM-dioxo	iPr	Ph

TABLE 3-continued



Compound No.	X, Y	R^2	R^3
3-375	4,5-diHM-dioxo	iPr	Ph
3-376	4,5-diHE-dioxo	iPr	Ph
3-377	dioxo	tBu	Ph
3-378	4-HM-dioxo	tBu	Ph
3-379	4,5-diHM-dioxo	tBu	Ph
3-380	4,5-diHE-dioxo	tBu	Ph
3-381	dioxo	CH_2OAc	Ph
3-382	4-HM-dioxo	CH_2OAc	Ph
3-383	4,5-diHM-dioxo	CH_2OAc	Ph
3-384	4,5-diHE-dioxo	CH_2OAc	Ph
3-385	dioxo	Me	4-F-Ph
3-386	4-HM-dioxo	Me	4-F-Ph
3-387	4,5-diHM-dioxo	Me	4-F-Ph
3-388	4,5-diHE-dioxo	Me	4-F-Ph
3-389	dioxo	nPr	4-F-Ph
3-390	4-HM-dioxo	nPr	4-F-Ph
3-391	4.5-diHM-dioxo	nPr	4-F-Ph
3-392	4,5-diHE-dioxo	nPr	4-F-Ph
3-393	dioxo	nBu	4-F-Ph
3-394	4-HM-dioxo	nBu	4-F-Ph
3-395	4,5-diHM-dioxo	nBu	4-F-Ph
3-396	4,5-diHE-dioxo	nBu	4-F-Ph
3-397	dioxo	iPr	4-F-Ph
3-398	4-HM-dioxo	iPr	4-F-Ph
3-399	4,5-diHM-dioxo	iPr	4-F-Ph
3-400	4,5-diHE-dioxo	iPr	4-F-Ph
3-401	dioxo	tBu	4-F-Ph
3-402	4-HM-dioxo	tBu	4-F-Ph
3-403	4,5-diHM-dioxo	tBu	4-F-Ph
3-404	4,5-diHE-dioxo	tBu	4-F-Ph
3-405	dioxo	CH_2OAc	4-F-Ph
3-406	4-HM-dioxo	CH_2OAc	4-F-Ph
3-407	4,5-diHM-dioxo	CH_2OAc	4-F-Ph
3-408	4,5-diHE-dioxo	CH_2OAc	4-F-Ph
3-409	dioxo	Me	2-Cl-4-Me-Ph
3-410	4-HM-dioxo	Me	2-Cl-4-Me-Ph
3-411	4,5-diHM-dioxo	Me	2-Cl-4-Me-Ph
3-412	4,5-diHE-dioxo	Me	2-Cl-4-Me-Ph
3-413	dioxo	nPr	2-Cl-4-Me-Ph
3-414	4-HM-dioxo	nPr	2-Cl-4-Me-Ph
3-415	4,5-diHM-dioxo	nPr	2-Cl-4-Me-Ph
3-416	4,5-diHE-dioxo	nPr	2-Cl-4-Me-Ph
3-417	dioxo	nBu	2-Cl-4-Me-Ph
3-418	4-HM-dioxo	nBu	2-Cl-4-Me-Ph
3-419	4,5-diHM-dioxo	nBu	2-Cl-4-Me-Ph
3-420	4,5-diHE-dioxo	nBu	2-Cl-4-Me-Ph
3-421	dioxo	iPr	2-Cl-4-Me-Ph
3-422	4-HM-dioxo	iPr	2-Cl-4-Me-Ph
3-423	4,5-diHM-dioxo	iPr	2-Cl-4-Me-Ph
3-424	4,5-diHE-dioxo	iPr	2-Cl-4-Me-Ph
3-425	dioxo	tBu	2-Cl-4-Me-Ph
3-426	4-HM-dioxo	tBu	2-Cl-4-Me-Ph
3-427	4,5-diHM-dioxo	tBu	2-Cl-4-Me-Ph
3-428	4,5-diHE-dioxo	tBu	2-Cl-4-Me-Ph
3-429	dioxo	CH_2OAc	2-Cl-4-Me-Ph
3-430	4-HM-dioxo	CH_2OAc	2-Cl-4-Me-Ph
3-431	4,5-diHM-dioxo	CH_2OAc	2-Cl-4-Me-Ph
3-432	4,5-diHE-dioxo	CH_2OAc	2-Cl-4-Me-Ph
3-433	dioxo	Me	2-nBu-Ph
3-434	4-HM-dioxo	Me	2-nBu-Ph
3-435	4,5-diHM-dioxo	Me	2-nBu-Ph
3-436	4,5-diHE-dioxo	Me	2-nBu-Ph
3-437	dioxo	nPr	2-nBu-Ph
3-438	4-HM-dioxo	nPr	2-nBu-Ph
3-439	4,5-diHM-dioxo	nPr	2-nBu-Ph
3-440	4,5-diHE-dioxo	nPr	2-nBu-Ph
3-441	dioxo	nBu	2-nBu-Ph

TABLE 3-continued



Compound No.	X, Y	R^2	R^3
3-442	4-HM-dioxo	nBu	2-nBu-Ph
3-443	4,5-diHM-dioxo	nBu	2-nBu-Ph
3-444	4,5-diHE-dioxo	nBu	2-nBu-Ph
3-445	dioxo	iPr	2-nBu-Ph
3-446	4-HM-dioxo	iPr	2-nBu-Ph
3-447	4,5-diHM-dioxo	iPr	2-nBu-Ph
3-448	4,5-diHE-dioxo	iPr	2-nBu-Ph
3-449	dioxo	tBu	2-nBu-Ph
3-450	4-HM-dioxo	tBu	2-nBu-Ph
3-451	4,5-diHM-dioxo	tBu	2-nBu-Ph
3-452	4,5-diHE-dioxo	tBu	2-nBu-Ph
3-453	dioxo	CH_2OAc	2-nBu-Ph
3-454	4-HM-dioxo	CH_2OAc	2-nBu-Ph
3-455	4,5-diHM-dioxo	CH_2OAc	2-nBu-Ph
3-456	4,5-diHE-dioxo	CH_2OAc	2-nBu-Ph
3-457	dioxo	Me	2-nPr-Ph
3-458	4-HM-dioxo	Me	2-nPr-Ph
3-459	4,5-diHM-dioxo	Me	2-nPr-Ph
3-460	4,5-diHE-dioxo	Me	2-nPr-Ph
3-461	dioxo	nPr	2-nPr-Ph
3-462	4-HM-dioxo	nPr	2-nPr-Ph
3-463	4,5-diHM-dioxo	nPr	2-nPr-Ph
3-464	4,5-diHE-dioxo	nPr	2-nPr-Ph
3-465	dioxo	nBu	2-nPr-Ph
3-466	4-HM-dioxo	nBu	2-nPr-Ph
3-467	4.5-diHM-dioxo	nBu	2-nPr-Ph
3-468	4,5-diHE-dioxo	nBu	2-nPr-Ph
3-469	dioxo	iPr	2-nPr-Ph
3-470	4-HM-dioxo	iPr	2-nPr-Ph
3-471	4,5-diHM-dioxo	iPr	2-nPr-Ph
3-472	4,5-diHE-dioxo	iPr	2-nPr-Ph
3-473	dioxo	tBu	2-nPr-Ph
3-474	4-HM-dioxo	tBu	2-nPr-Ph
3-475	4,5-diHM-dioxo	tBu	2-nPr-Ph
3-476	4,5-diHE-dioxo	tBu	2-nPr-Ph
3-477	dioxo	CH_2OAc	2-nPr-Ph
3-478	4-HM-dioxo	CH_2OAc	2-nPr-Ph
3-479	4,5-diHM-dioxo	CH_2OAc	2-nPr-Ph
3-480	4,5-diHE-dioxo	CH_2OAc	2-nPr-Ph
3-481	dioxo	Me	4-F-2-nPr-Ph
3-482	4-HM-dioxo	Me	4-F-2-nPr-Ph
3-483	4,5-diHM-dioxo	Me	4-F-2-nPr-Ph
3-484	4,5-diHE-dioxo	Me	4-F-2-nPr-Ph
3-485	dioxo	nPr	4-F-2-nPr-Ph
3-486	4-HM-dioxo	nPr	4-F-2-nPr-Ph
3-487	4,5-diHM-dioxo	nPr	4-F-2-nPr-Ph
3-488	4,5-diHE-dioxo	nPr	4-F-2-nPr-Ph
3-489	dioxo	nBu	4-F-2-nPr-Ph
3-490	4-HM-dioxo	nBu	4-F-2-nPr-Ph
3-491	4,5-diHM-dioxo	nBu	4-F-2-nPr-Ph
3-492	4,5-diHE-dioxo	nBu	4-F-2-nPr-Ph
3-493	dioxo	iPr	4-F-2-nPr-Ph
3-494	4-HM-dioxo	iPr	4-F-2-nPr-Ph
3-495	4,5-diHM-dioxo	iPr	4-F-2-nPr-Ph
3-496	4,5-diHE-dioxo	iPr	4-F-2-nPr-Ph
3-497	dioxo	tBu	4-F-2-nPr-Ph
3-498	4-HM-dioxo	tBu	4-F-2-nPr-Ph
3-499	4,5-diHM-dioxo	tBu	4-F-2-nPr-Ph
3-500	4,5-diHE-dioxo	tBu	4-F-2-nPr-Ph
3-501	dioxo	CH_2OAc	4-F-2-nPr-Ph
3-502	4-HM-dioxo	CH_2OAc	4-F-2-nPr-Ph
3-503	4,5-diHM-dioxo	CH_2OAc	4-F-2-nPr-Ph
3-504	4,5-diHE-dioxo	CH_2OAc	4-F-2-nPr-Ph

In the compounds having the general formula (I) of the present invention, as preferred compounds exemplified compound Nos.: 1-12, 1-13, 1-19, 1-20, 1-26, 1-28, 1-30, 1-32,

1-34, 1-36, 1-38, 1-40, 1-42, 1-44, 1-46, 1-48, 1-50, 1-54, 1-58, 1-60, 1-62, 1-66, 1-68, 1-70, 1-72, 1-74, 1-78, 1-80, 1-82, 1-86, 1-100, 1-101, 1-107, 1-108, 1-114, 1-116, 1-118, 1-120, 1-122, 1-124, 1-126, 1-128, 1-130, 1-132, 1-134, 1-136, 1-138, 1-142, 1-146, 1-148, 1-150, 1-154, 1-156, 1-158, 1-160, 1-162, 1-166, 1-168, 1-170, 1-174, 1-188, 1-189, 1-195, 1-196, 1-202, 1-204, 1-206, 1-208, 1-210, 1-212, 1-214, 1-216, 1-218, 1-220, 1-222, 1-224, 1-226, 1-230, 1-234, 1-236, 1-238, 1-242, 1-244, 1-246, 1-248, 1-250, 1-254, 1-256, 1-258, 1-262, 1-276, 1-277, 1-283, 1-284, 1-290, 1-292, 1-294, 1-296, 1-298, 1-300, 1-302, 1-304, 1-306, 1-308, 1-310, 1-312, 1-314, 1-318, 1-322, 1-324, 1-326, 1-330, 1-332, 1-334, 1-336, 1-338, 1-342, 1-344, 1-346, 1-350, 1-353, 1-355, 1-360 to 1-369, 1-371, 1-372, 1-378, 1-380, 1-382, 1-384, 1-386, 1-388, 1-390, 1-392, 1-394, 1-396, 1-398, 1-400, 1-402, 1-406, 1-410, 1-412, 1-414, 1-418, 1-420, 1-422, 1-424, 1-426, 1-430, 1-432, 1-434, 1-438, 1-452, 1-453, 1-459, 1-460, 1-466, 1-468, 1-470, 1-472, 1-474, 1-476, 1-478, 1-480, 1-482, 1-484, 1-486, 1-488, 1-490, 1-494, 1-498, 1-500, 1-502, 1-506, 1-508, 1-510, 1-512, 1-514, 1-518, 1-520, 1-522, 1-526, 1-540, 1-541, 1-547, 1-548, 1-554, 1-556, 1-558, 1-560, 1-562, 1-564, 1-566, 1-568, 1-570, 1-572, 1-574, 1-576, 1-578, 1-582, 1-586, 1-588, 1-590, 1-594, 1-596, 1-598, 1-600, 1-602, 1-604, 1-606, 1-608, 1-610, 1-614, 1-628, 1-629, 1-635, 1-636, 1-642, 1-644, 1-646, 1-648, 1-650, 1-652, 1-654, 1-656, 1-658, 1-660, 1-662, 1-664, 1-666, 1-670, 1-674, 1-676, 1-678, 1-682, 1-684, 1-686, 1-688, 1-690, 1-694, 1-696, 1-698, 1-702, 1-712 to 1-720, 1-723, 1-724, 1-730, 1-732, 1-734, 1-736, 1-738, 1-740, 1-742, 1-744, 1-746, 1-748, 1-750, 1-752, 1-754, 1-758, 1-762, 1-764, 1-766, 1-770, 1-772, 1-774, 1-776, 1-778, 1-782, 1-784, 1-786, 1-790, 1-804, 1-805, 1-811, 1-812, 1-818, 1-820, 1-822, 1-824, 1-826, 1-828, 1-830, 1-832, 1-834, 1-836, 1-838, 1-840, 1-842, 1-846, 1-850, 1-852, 1-854, 1-858, 1-860, 1-862, 1-864, 1-866, 1-870, 1-872, 1-874, 1-878, 1-888 to 1-896, 1-899, 1-900, 1-906, 1-908, 1-910, 1-912, 1-914, 1-916, 1-918, 1-920, 1-922, 1-924, 1-926, 1-928, 1-930, 1-934, 1-938, 1-940, 1-942, 1-946, 1-948, 1-950, 1-952, 1-954, 1-958, 1-960, 1-962, 1-966, 1-980, 1-981, 1-987, 1-988, 1-994, 1-996, 1-998, 1-1000, 1-1002, 1-1004, 1-1006, 1-1008, 1-1010, 1-1012, 1-1014, 1-1016, 1-1018, 1-1022, 1-1026, 1-1028, 1-1030, 1-1034, 1-1036, 1-1038, 1-1040, 1-1042, 1-1046, 1-1048, 1-1050, 1-1054, 1-1057, 1-1062, 1-1063, 1-1066, 1-1067 to 1-1070, 1-1074, 1-1079, 1-1080, 1-1083, 1-1085 to 1-1087, 1-1091, 1-1096, 1-1097, 1-1100, 1-1102 to 1-1104, 1-1108, 1-1113, 1-1114, 1-1117, 1-1119 to 1-1121, 1-1125, 1-1130, 1-1131, 1-1134, 1-1136 to 1-1138, 1-1142, 1-1147, 1-1148, 1-1151, 1-1153 to 1-1155, 1-1159, 1-1164, 1-1165, 1-1168, 1-1170 to 1-1172, 1-1176, 1-1181, 1-1182, 1-1185, 1-1187 to 1-1189, 1-1193, 1-1198, 1-1199, 1-1202, 1-1204 to 1-1206, 1-1210, 1-1215, 1-1216, 1-1219, 1-1221 to 1-1223, 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1-2350 to 1-2354, 1-2357 to 1-2361, 1-2364 to 1-2368, 1-2371 to 1-2375, 1-2378 to 1-2382, 1-2385 to 1-2389, 1-2392 to 1-2396, 1-2399 to 1-2403, 1-2406 to 1-2410, 1-2413 to 1-2417, 1-2420 to 1-2424, 1-2427 to 1-2431, 1-2434 to 1-2438, 1-2441 to 1-2445, 1-2448 to 1-2452, 1-2455 to 1-2459, 1-2462 to 1-2466, 1-2469 to 1-2473, 1-2476 to 1-2480, 1-2483 to 1-2487, 1-2490 to 1-2494, 1-2497 to 1-2501, 1-2504 to 1-2508, 1-2511 to 1-2515, 1-2518 to 1-2522, 1-2525 to 1-2529, 1-2532 to 1-2536, 1-2539 to 1-2543, 1-2546 to 1-2550, 1-2553 to 1-2557, 1-2560 to 1-2564, 1-2567 to 1-2571, 1-2574 to 1-2578, 1-2581 to 1-2585, 1-2588 to 1-2592, 1-2595 to 1-2599, 1-2602 to 1-2606, 1-2609 to 1-2613, 1-2616 to 1-2620, 1-2623 to 1-2627, 2-3, 2-4, 2-7, 2-8, 2-11, 2-12, 2-15, 2-16, 2-19, 2-20, 2-23, 2-24, 2-27, 2-28, 2-31, 2-32, 2-35, 2-36, 2-39, 2-40, 2-43, 2-44, 2-47, 2-48, 2-51, 2-52, 2-59, 2-60, 2-83, 2-84, 3-3, 3-4, 3-7, 3-8, 3-11, 3-12, 3-15, 3-16, 3-27, 3-28, 3-31, 3-32, 3-35, 3-36, 3-39, 3-40, 3-51, 3-52, 3-55, 3-56, 3-59, 3-60, 3-63, 3-64, 3-75, 3-76, 3-79, 3-80, 3-83, 3-84, 3-87, 3-88, 3-99, 3-100, 3-103, 3-104, 3-107, 3-108, 3-111, 3-112, 3-123, 3-124, 3-127, 3-128, 3-131, 3-132, 3-135, 3-136, 3-147, 3-148, 3-151, 3-152, 3-155, 3-156, 3-159, 3-160, 3-171, 3-172, 3-175, 3-176, 3-179, 3-180, 3-183, 3-184, 3-195, 3-196, 3-199, 3-200, 3-203, 3-204, 3-207, 3-208, 3-219, 3-220, 3-223, 3-224, 3-227, 3-228, 3-231, 3-232, 3-243, 3-244, 3-247, 3-248, 3-251, 3-252, 3-255, 3-256, 3-267, 3-268, 3-271, 3-272, 3-275, 3-276, 3-279, 3-280, 3-291, 3-292, 3-295, 3-296, 3-299,

3-300, 3-303, 3-304, 3-339, 3-340, 3-343, 3-344, 3-347, 3-348, 3-351, 3-352, 3-483, 3-484, 3-487, 3-488, 3-491, 3-492, 3-495, and 3-496 can be mentioned,

more preferably, exemplified compound Nos.: 1-12, 1-26, 1-30, 1-34, 1-38, 1-42, 1-46, 1-58, 1-66, 1-70, 1-78, 1-100, 1-114, 1-118, 1-122, 1-126, 1-130, 1-134, 1-146, 1-154, 1-158, 1-166, 1-188, 1-202, 1-206, 1-210, 1-214, 1-218, 1-222, 1-234, 1-242, 1-246, 1-254, 1-276, 1-290, 1-294, 1-298, 1-302, 1-306, 1-310, 1-322, 1-330, 1-334, 1-342, 1-364, 1-378, 1-382, 1-386, 1-390, 1-394, 1-398, 1-410, 1-418, 1-422, 1-430, 1-452, 1-466, 1-470, 1-474, 1-478, 1-482, 1-486, 1-498, 1-506, 1-510, 1-518, 1-540, 1-554, 1-558, 1-562, 1-566, 1-570, 1-574, 1-586, 1-594, 1-598, 1-604, 1-606, 1-628, 1-642, 1-646, 1-650, 1-654, 1-658, 1-662, 1-674, 1-682, 1-686, 1-694, 1-716, 1-730, 1-734, 1-738, 1-742, 1-746, 1-750, 1-762, 1-770, 1-774, 1-782, 1-804, 1-818, 1-822, 1-826, 1-830, 1-834, 1-838, 1-850, 1-858, 1-862, 1-870, 1-892, 1-906, 1-910, 1-914, 1-918, 1-922, 1-926, 1-938, 1-946, 1-950, 1-958, 1-980, 1-994, 1-998, 1-1002, 1-1006, 1-1010, 1-1014, 1-1026, 1-1034, 1-1038, 1-1046, 1-1227, 1-1232, 1-1239, 1-1240, 1-1244, 1-1249, 1-1256, 1-1257, 1-1261, 1-1266, 1-1273, 1-1274, 1-1278, 1-1283, 1-1290, 1-1291, 1-1295, 1-1300, 1-1307, 1-1308, 1-1374, 1-1388, 1-1392, 1-1396, 1-1400, 1-1404, 1-1408, 1-1420, 1-1428, 1-1432, 1-1440, 1-1462, 1-1476, 1-1480, 1-1484, 1-1488, 1-1492, 1-1496, 1-1508, 1-1516, 1-1520, 1-1528, 1-1550, 1-1564, 1-1568, 1-1572, 1-1576, 1-1580, 1-1584, 1-1596, 1-1604, 1-1608, 1-1616, 1-1638, 1-1652, 1-1656, 1-1660, 1-1664, 1-1668, 1-1672, 1-1684, 1-1692, 1-1696, 1-1704, 1-1726, 1-1740, 1-1744, 1-1748, 1-1752, 1-1756, 1-1760, 1-1772, 1-1780, 1-1784, 1-1792, 1-1814, 1-1828, 1-1832, 1-1836, 1-1840, 1-1844, 1-1848, 1-1860, 1-1868, 1-1872, 1-1880, 1-1902, 1-1916, 1-1920, 1-1924, 1-1928, 1-1932, 1-1936, 1-1948, 1-1956, 1-1960, 1-1968, 1-1989, 1-2003, 1-2007, 1-2011, 1-2015, 1-2019, 1-2023, 1-2035, 1-2043, 1-2047, 1-2055, 1-2077, 1-2091, 1-2095, 1-2099, 1-2103, 1-2107, 1-2111, 1-2123, 1-2131, 1-2135, 1-2143, 1-2219, 1-2220, 1-2226, 1-2227, 1-2233, 1-2234, 1-2240, 1-2241, 1-2247, 1-2248, 1-2254, 1-2255, 1-2261, 1-2262, 1-2268, 1-2269, 1-2275, 1-2276, 1-2282, 1-2283, 1-2289, 1-2290, 1-2296, 1-2297, 1-2303, 1-2304, 1-2310, 1-2311, 1-2317, 1-2318, 1-2324, 1-2325, 1-2331, 1-2332, 1-2338, 1-2339, 1-2345, 1-2346, 1-2352, 1-2353, 1-2359, 1-2360, 1-2366, 1-2367, 1-2373, 1-2374, 1-2380, 1-2381, 1-2387, 1-2388, 1-2394, 1-2395, 1-2401, 1-2402, 1-2408, 1-2409, 1-2415, 1-2416, 1-2422, 1-2423, 1-2429, 1-2430, 1-2436, 1-2437, 1-2443, 1-2444, 1-2450, 1-2451, 1-2457, 1-2458, 1-2464, 1-2465, 1-2471, 1-2472, 1-2478, 1-2479, 1-2485, 1-2486, 1-2492, 1-2493, 1-2499, 1-2500, 1-2506, 1-2507, 1-2513, 1-2514, 1-2520, 1-2521, 1-2527, 1-2528, 1-2534, 1-2535, 1-2541, 1-2542, 1-2548, 1-2549, 1-2555, 1-2556, 1-2562, 1-2563, 1-2569, 1-2570, 1-2576, 1-2577, 1-2583, 1-2584, 1-2590, 1-2591, 1-2597, 1-2598, 1-2604, 1-2605, 1-2611, 1-2612, 1-2618, 1-2619, 1-2625, 1-2626, 2-3, 2-7, 2-11, 2-15, 2-19, 2-23, 2-27, 2-31, 2-35, 2-39, 2-43, 2-47, 2-51, 2-59, 2-83, 3-7, 3-31, 3-55, 3-79, 3-103, 3-127, 3-151, 3-175, 3-199, 3-223, 3-247, 3-271, 3-295, 3-343 and 3-487can be mentioned,

even more preferably,

exemplified compound No. 1-206: ethyl 8-[N-(2-chlorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-210: ethyl 8-[N-(2-chlorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-294: ethyl 8-[N-(2,4-difluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-298: ethyl 8-[N-(2,4-difluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-378: ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-hydroxymethyl-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-382: ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-386: ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-390: ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-394: ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-(1,2,3-trihydroxypropyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-398: ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-(1,2,3,4-tetrahydroxybutyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-410: ethyl 2,3-bis(acetylaminomethyl)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-418: ethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3-hydroxy-1,5-dioxaspiro[5.5]undec-7-ene-8-carboxylate,

exemplified compound No. 1-422: ethyl 3-acetylamino-9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,5-dioxaspiro[5.5]undec-7-ene-8-carboxylate,

exemplified compound No. 1-430: ethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-bis(hydroxymethyl)-1,5-dioxaspiro[5.5] undec-7-ene-8-carboxylate,

exemplified compound No. 1-646: ethyl 8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-650: ethyl 8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-734: ethyl 8-[N-(2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-738: ethyl 8-[N-(2-hexyl phenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-822: ethyl 8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-826: ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-910: ethyl 8-[N-(2-heptylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-914: ethyl 8-[N-(2-heptylphenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-998: ethyl 8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-1002: ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-1392: ethyl 8-[N-(2-bromophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-1396: ethyl 8-[N-(2-bromophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-1480: ethyl 8-[N-(2-chloro-6-methylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-1484: ethyl 8-[N-(2-chloro-6-methylphenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-1568: ethyl 8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-1572: ethyl 8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-1656: ethyl 2,3-bis(hydroxymethyl)-8-[N-(2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-1660: ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-1744: ethyl 8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-1748: ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-1920: ethyl 8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-1924: ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-2095: ethyl 8-[N-(4-fluoro-2-propylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

exemplified compound No. 1-2099: ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-propylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate

and

exemplified compound No. 2-15: ethyl 8-[N-(2-chloro-4-fluorophenyl)-N-methylsulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate can be mentioned.

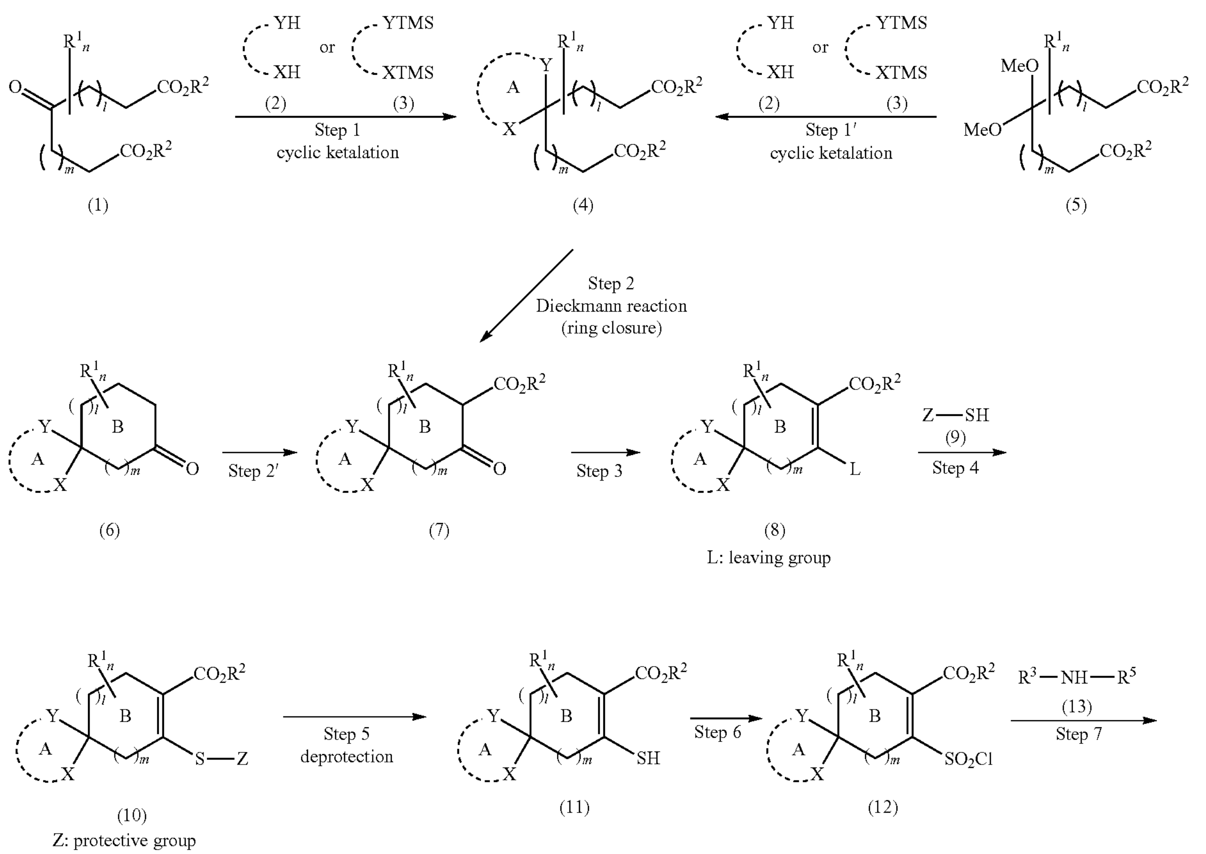
The compound having the general formula (I) according to the present invention can easily be prepared in accordance with Method A to Method C shown hereafter.

Method A is a method to prepare a compound having the general formula (I), by introducing a cyclic ketal in the initial stage of the preparation.

Method B is a method to prepare a compound having the general formula (I), by introducing a cyclic ketal in the final stage of the preparation.

Method C is a method to prepare a compound having the general formula (I), by introducing R^5 in the final stage of the preparation.

Method A



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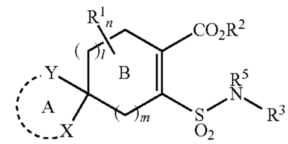
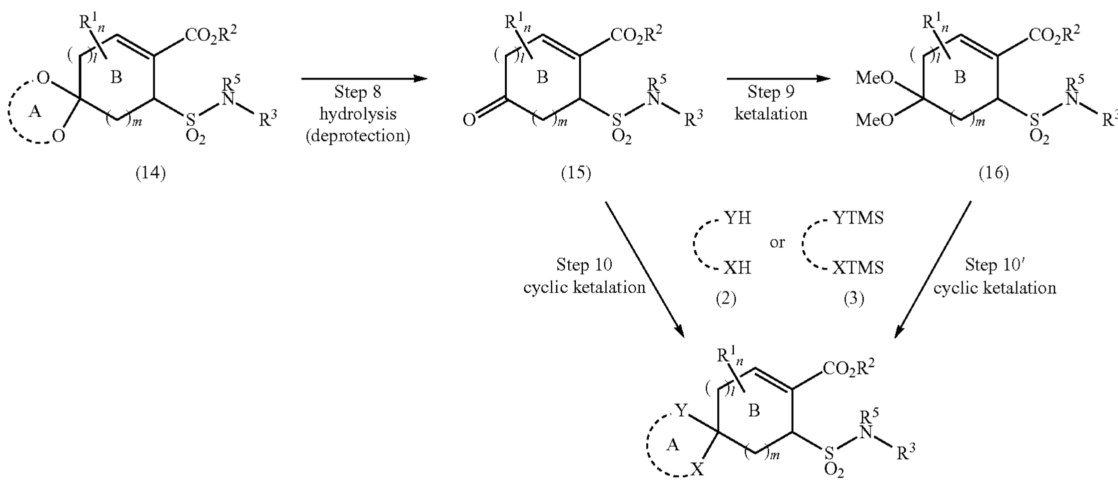


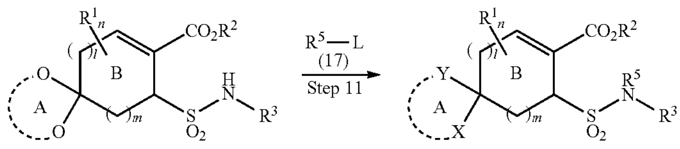
(I)

Method B



(I)

Method C



(14) or (I)′ (I)

In the aforementioned Method A to Method C, ring A, ring B, X, Y, R^1, R^2, R^3, R^5, m and n have the same meanings as defined above, L represents a leaving group and Z represents a protective group.

In the reactions of Method A to Method C, in the case where the compound as the reactive substrate has a group such as an amino group, hydroxy group and/or carboxyl group, which inhibits the intended reaction, these groups may be protected with a protective group as necessary. The protective group of a group which inhibits the intended reaction is not limited so long as it is a protective group which is ordinarily used to conduct the reaction, and may be, for example, a protective w group described in “Protective Groups in Organic Synthesis, 3rd edition, T. W. Greene & P. G. M. Wuts; John Wiley & Sons, Inc.”

A protective group of an amino group can be used without particular limitation so long as it is a group generally used as a protective group of an amino group, and preferably, formyl, the aforementioned C_1-C_6 alkylcarbonyl group; the aforementioned arylcarbonyl group; the aforementioned C_1-C_6 alkoxycarbonyl group; the aforementioned C_1-C_6 alkanoyl group which is substituted with halogen; aralkyl groups such as benzyl, phenethyl, 3-phenylpropyl, 4-phenylbutyl, α-naphthylmethyl, β-naphthylmethyl, diphenylmethyl, triphenylmethyl, α-naphthyldiphenylmethyl or 9-anthrylmethyl; the aforementioned aralkyloxycarbonyl group and the like can be mentioned.

A protective group of a hydroxy group can be used without particular limitation so long as it is a group generally used as a protective group of a hydroxy group, and preferably, formyl, C_1-C_6 alkylcarbonyl groups such as acetyl, arylcarbonyls such as benzoyl group; and alkoxylated alkoxymethyls such as 2-methoxyethoxymethyl can be mentioned.

A protective group of a carboxyl group can be used without particular limitation so long as it is a group generally used as a protective group of a carboxyl group, and preferably, the aforementioned C_1-C_6 alkyl group; and aralkyl groups such as benzyl, phenethyl and phenylpropyl can be mentioned.

Further, these protective groups of groups which inhibit the intended reaction may be cleaved as necessary. The cleavage reaction of these protective groups, which is the desired reaction, may be conducted in accordance with conventional procedures which are used in the field of synthetic organic chemistry (for example, the procedure described in the aforementioned Protective Groups in Organic Synthesis, 3rd edition, T. W. Greene & P. G. M. Wuts; John Wiley & Sons, Inc).

<Method A>

Step 1 of Method A is a step to react a ketone compound (1) with a compound (2) or a compound (3), which is compound (2) having its terminal substituted with a trimethylsilyl group (described as TMS in the aforementioned scheme), in an inert solvent in the presence of acid, to prepare a cyclic ketal compound (4).

This step can adopt a cyclic ketalation reaction (protection) of a ketone, which is widely used in general organic synthesis, and can be conducted in accordance with the procedure described in T. W. Greene, P. C. Wuts, Protective Groups in organic Synthesis. Third Edition, 1999, Chapter 4, pp. 293-368, John Wiley & Sons, Inc. and the like, or in accordance with similar procedures.

Here, the cyclic ketal compound (4) can also be prepared by the following procedure (Step 1' of Method A).

Step 1' of Method A is a step to react a dimethylketal compound (5) with compound (2) or compound (3), in an inert solvent in the presence of acid, to prepare a cyclic ketal compound (4). This reaction can be conducted in accordance with the same procedure as or based on the procedure of Step 1.

Step 2 of Method A is a step to allow the cyclic ketal compound (4) obtained by Step 1 or Step 1' to undergo a Dieckmann reaction, to prepare a ketoester compound (7).

This step can adopt a Dieckmann reaction which is widely used generally in organic synthesis, and can be conducted in accordance with the procedure described in Chemical Pharmaceutical Bulletin (Chem. Pharm. Bull.) Vol. 29, pp. 3238-3248 (1981) and the like, or based on that procedure.

Here, the ketoester compound (7) can also be prepared by the following procedure (Step 2' of Method A).

Step 2' of Method A is a step to react a ketone compound (6) with a dialkyl carbonate, in an inert solvent in the presence of base, to prepare a ketoester compound (7).

This step can adopt an ester group introducing reaction which is widely used generally in organic synthesis, and can be conducted in accordance with the procedure described in Canadian Journal of Chemistry (Can. J. Chem.) Vol. 70, pp. 1406-1426 (1992) and the like, or based on that procedure.

Step 3 of Method A is a step to enolate the ketoester compound (7) obtained in Step 2 or Step 2', in an inert solvent in the presence of base, to prepare a compound (8) having a leaving group L.

This step can be conducted in accordance with the procedure described in Journal of American Chemical Society (J. Am. Chem. Soc.), Vol. 120, pp. 3664-3670 (1998) and the like, or based on that procedure.

"Leaving group" in the definition of L generally represents a group which leaves as a nucleophilic residue, and for example, halogen atoms such as a fluorine atom, chlorine atom, bromine atom and iodine atom; lower alkanesulfonyloxy groups such as methanesulfonyloxy and ethanesulfonyloxy; halogeno lower alkanesulfonyloxy groups such as trifluoromethanesulfonyloxy and pentafluoroethanesulfonyloxy; and arylsulfonyloxy groups such as benzenesulfonyloxy, p-toluenesulfonyloxy and p-nitrobenzenesulfonyloxy can be mentioned. Preferably, it is a halogeno lower alkanesulfonyloxy group, particularly preferably a trifluoromethanesulfonyloxy group.

The inert solvent used is not particularly limited so long as it does not inhibit the reaction and dissolves the starting material to some degree, and for example, aromatic hydrocarbons such as benzene, toluene and xylene; halogenated hydrocarbons such as dichloromethane, chloroform, carbon tetrachloride, dichloroethane, chlorobenzene and dichlorobenzene; ethers such as diethyl ether, diisopropyl ether, tetrahydrofuran, dioxane, dimethoxyethane and diethyleneglycoldimethyl ether; amides such as formamide, N,N-dimethylformamide, N,N-dimethylacetamide, N-methyl-2-pyrrolidinone and hexamethylphosphorotriamide; or a solvent mixture of these can be mentioned. Preferably, it is a halogenated hydrocarbon, more preferably dichloromethane.

The base used includes inorganic bases such as alkali metal carbonates such as sodium carbonate, potassium carbonate and lithium carbonate; alkali metal hydrogen carbonates such as sodium hydrogen carbonate, potassium hydrogen carbonate and lithium hydrogen carbonate; alkali metal hydrides such as lithium hydride, sodium hydride and potassium hydride; alkali metal fluorides such as sodium fluoride and potassium fluoride; organic bases such as alkali metal alkoxides such as sodium methoxide, sodium ethoxide, potassium methoxide, potassium ethoxide, potassium t-butoxide and lithium methoxide; N-methylmorpholine, triethylamine, tripropylamine, tributylamine, diisopropylethylamine, dicyclohexylamine, N-methylpiperidine, pyridine, 4-pyrrolidinopyridine, picoline, 4-(N,N-dimethylamino)pyridine, 2,6-di (t-butyl)-4-methylpyridine, quinoline, N,N-dimethylaniline, N,N-diethylaniline, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,4-diazabicyclo[2.2.2]octane (DABCO) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), preferably alkali metal hydrides or organic bases, and more preferably sodium hydride or diisopropylethylamine.

Reaction temperature varies depending on the starting compound and reaction reagent, and the reaction is conducted from −100° C. to 100° C., preferably from −78° C. to 50° C.

Reaction time varies depending on the reaction temperature, starting compound, reaction reagent or the type of solvent used, and it is generally in the range from 1 minute to 48 hours, preferably from 5 minutes to 12 hours.

Step 4 of Method A is a step to react the compound (8) having a leaving group L obtained in Step 3 with a thiol compound (9) in an inert solvent in the presence of a base, to prepare compound (10).

"Protective group" of the sulfanyl group in the definition of Z is not particularly limited so long as it is a protective group of a sulfanyl group which is widely used generally in organic synthesis, and alkanoyl groups such as formyl, acetyl, propionyl and butyryl, and arylcarbonyl groups such as benzoyl, α-naphthoyl, β-naphthoyl, pyridoyl, thienoyl and furoyl can be mentioned, for example. Preferably, it is a group which forms a pharmacologically acceptable ester, and is more preferably an acetyl group.

The inert solvent used is not particularly limited so long as it does not inhibit the reaction and dissolves the starting material to some degree, and for example, aromatic hydrocarbons such as benzene, toluene and xylene; halogenated hydrocarbons such as dichloromethane, chloroform, carbon tetrachloride, dichloroethane, chlorobenzene and dichlorobenzene; ethers such as diethyl ether, diisopropyl ether, tetrahydrofuran, dioxane, dimethoxyethane and diethyleneglycoldimethyl ether; aprotic polar solvents such as formamide, N,N-dimethylformamide, N,N-dimethylacetamide and dimethyl sulfoxide; or a solvent mixture of these can be mentioned. Preferably, it is an aprotic polar solvent, more preferably N,N-dimethylformamide.

The base used includes inorganic bases such as alkali metal carbonates, e.g. sodium carbonate, potassium carbonate and lithium carbonate; alkali metal hydrogen carbonates such as sodium hydrogen carbonate, potassium hydrogen carbonate and lithium hydrogen carbonate; alkali metal hydrides such as lithium hydride, sodium hydride and potassium hydride; alkali metal fluorides such as sodium fluoride and potassium fluoride; organic bases such as alkali metal alkoxides, e.g. sodium methoxide, sodium ethoxide, potassium methoxide, potassium ethoxide, potassium t-butoxide and lithium methoxide; N-methylmorpholine, triethylamine, tripropylamine, tributylamine, diisopropylethylamine, dicyclohexylamine, N-methylpiperidine, pyridine, 4-pyrrolidinopyridine, picoline, 4-(N,N-dimethylamino)pyridine, 2,6-di(t-butyl)-4-

methylpyridine, quinoline, N,N-dimethylaniline, N,N-diethylaniline, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,4-diazabicyclo[2.2.2]octane (DABCO) and 1,8-diazabicyclo [5.4.0]undec-7-ene (DBU) can be mentioned, and is preferably an alkali metal hydride, more preferably sodium hydride or potassium hydride.

Reaction temperature varies depending on the starting compound and reaction reagent, and the reaction is conducted from −78° C. to 100° C., preferably from −20° C. to 50° C.

Reaction time varies depending on the reaction temperature, starting compound, reaction reagent or the type of solvent used, and it is generally in the range from 1 minute to 120 hours, preferably from 10 minutes to 72 hours.

Step 5 of Method A is a step to deprotect the protective group of the sulfanyl group of the compound (10) obtained in Step 4, in an inert solvent, to prepare compound (11).

This step is a deprotection step of a protective group of a sulfanyl group which is widely used in general organic synthesis, and is conducted in accordance with the procedure described in the aforementioned "Protective Groups in Organic Synthesis, 3rd edition, T. W. Greene & P. G. M. Wuts; John Wiley & Sons, Inc." and the like, or based on that procedure, and can be preferably conducted by a deprotection procedure in an inert solvent in the presence of base.

The inert solvent used is not particularly limited so long as it does not inhibit the reaction and dissolves the starting material to some degree, and for example, aromatic hydrocarbons such as benzene, toluene and xylene; halogenated hydrocarbons such as dichloromethane, chloroform, carbon tetrachloride, dichloroethane, chlorobenzene and dichlorobenzene; ethers such as diethyl ether, diisopropyl ether, tetrahydrofuran, dioxane, dimethoxyethane and diethyleneglycoldimethyl ether; alcohols such as methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, t-butanol, isoamyl alcohol, diethylene glycol, glycerin, octanol, cyclohexanol and 2-methoxyethanol; amides such as formamide, N,N-dimethylformamide, N,N-dimethylacetamide, N-methyl-2-pyrrolidinone and hexamethylphosphortriamide; sulfoxides such as dimethyl sulfoxide and sulfolane; or a solvent mixture of these can be mentioned, and is preferably an alcohol, and more preferably methanol or ethanol.

The base used includes alkali metal carbonates such as sodium carbonate, potassium carbonate and lithium carbonate; alkali metal hydrogen carbonates such as sodium hydrogencarbonate, potassium hydrogencarbonate and lithium hydrogencarbonate; organic bases such as alkali metal alkoxides, e.g. sodium methoxide, sodium ethoxide, potassium methoxide, potassium ethoxide, potassium t-butoxide and lithium methoxide; N-methylmorpholine, triethylamine, tripropylamine, tributylamine, diisopropylethylamine, dicyclohexylamine, N-methylpiperidine, pyridine, 4-pyrrolidinopyridine, picoline, 4-(N,N-dimethylamino)pyridine, 2,6-di (t-butyl)-4-methylpyridine, quinoline, N,N-dimethylaniline, N,N-diethylaniline, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,4-diazabicyclo[2.2.2]octane (DABCO) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), preferably alkali metal carbonates, and more preferably potassium carbonate.

Reaction temperature varies depending on the starting compound and reaction reagent, and the reaction is conducted from −78° C. to 100° C., preferably from −20° C. to 50° C.

Reaction time varies depending on the reaction temperature, starting compound, reaction reagent or the type of solvent used, and it is generally from 1 minute to 24 hours, preferably from 5 minutes to 5 hours.

Step 6 of Method A is a step to chlorosulfonylate the thiol group of the compound (11) obtained in Step 5, in an inert solvent, to prepare compound (12).

This step can be conducted in accordance with the procedure described in Journal of Organic Chemistry (J. Org. Chem.), Vol. 16, pp. 621-625 (1951) and the like, or based on that procedure.

The inert solvent used is not particularly limited so long as it does not inhibit the reaction and dissolves the starting material to some degree, and for example, aromatic hydrocarbons such as benzene, toluene and xylene; halogenated hydrocarbons such as dichloromethane, chloroform, carbon tetrachloride and dichloroethane; ethers such as diethyl ether, diisopropyl ether, tetrahydrofuran, dioxane, dimethoxyethane and diethyleneglycoldimethyl ether; alcohols such as methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, t-butanol, isoamyl alcohol, diethylene glycol, glycerin, octanol, cyclohexanol and 2-methoxyethanol; aprotic polar solvents such as N, N-dimethylformamide, N,N-dimethylacetamide and dimethyl sulfoxide; nitrites such as acetonitrile; esters such as methyl acetate and ethyl acetate; carboxylic acids such as formic acid, acetic acid, propionic acid and trifluoroacetic acid; water; or a solvent mixture of these can be mentioned. Preferably, it is a solvent mixture of carboxylic acids and water or a solvent mixture of nitrites and water, more preferably a solvent mixture of acetic acid and water, or a solvent mixture of acetonitrile and water.

Reaction temperature varies according to the starting compound and reaction reagent, and the reaction is conducted from −78° C. to 100° C., preferably from −20° C. to 50° C.

Reaction time varies depending on the reaction temperature, starting compound, reaction reagent or the type of solvent used, and it is generally from 1 minute to 12 hours, preferably from 5 minutes to 1 hour.

Step 7 of Method A is a step to react the compound (12) obtained in Step 6 with an amine compound (13) in an inert solvent in the presence or absence of base, to prepare a compound of general formula (I).

The inert solvent used is not particularly limited so long as it does not inhibit the reaction and dissolves the starting material to some degree, and for example, aromatic hydrocarbons such as benzene, toluene and xylene; halogenated hydrocarbons such as dichloromethane, chloroform, carbon tetrachloride and dichloroethane; ethers such as diethyl ether, diisopropyl ether, tetrahydrofuran, dioxane, dimethoxyethane and diethyleneglycoldimethyl ether; aprotic polar solvents such as N,N-dimethylformamide, N,N-dimethylacetamide and dimethyl sulfoxide; nitrites such as acetonitrile; esters such as methyl acetate and ethyl acetate; or a solvent mixture of these can be mentioned. Preferably, it is an ester, more preferably ethyl acetate.

The base used includes alkali metal hydrates such as lithium hydrate, sodium hydrate and potassium hydrate; organic bases such as N-methylmorpholine, triethylamine, tripropylamine, tributylamine, diisopropylethylamine, dicyclohexylamine, N-methylpiperidine, pyridine, 4-pyrrolidinopyridine, picoline, 4-(N,N-dimethylamino)pyridine, 2,6-di (t-butyl)-4-methylpyridine, quinoline, N,N-dimethylaniline, N,N-diethylaniline, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,4-diazabicyclo[2.2.2]octane (DABCO) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), preferably organic bases, and more preferably triethylamine.

Reaction temperature varies depending on the starting compound and reaction reagent, and the reaction is conducted from −78° C. to 100° C., preferably from −20° C. to 50° C.

Reaction time varies depending on the reaction temperature, starting compound, reaction reagent or the type of solvent used, and it is generally in the range from 1 minute to 120 hours, preferably from 10 minutes to 48 hours.

<Method B>

Step 8 of Method B is a step to hydrolyze the cyclic ketal compound (14) obtained in Method A in an inert solvent in the presence of acid, to prepare a ketone compound (15).

This step can adopt a deprotection reaction of a cyclic ketal compound which is widely used generally in organic synthesis, and can be conducted in accordance with the procedure described in the aforementioned T. W. Greene, O. G. Wuts, Protective Groups in Organic Synthesis. Third Edition, 1999, Chapter 4, pp. 293-368, John Wiley & Sons, Inc. and the like, or based on that procedure.

Step 9 of Method B is a step to prepare a dimethylketal compound (16) with the ketone compound (15) obtained in Step 8 in an inert solvent in the presence of acid.

This step can adopt a dimethylketalation reaction (protection) of a ketone which is widely used generally in organic synthesis, and can be conducted in accordance with the procedure described in the aforementioned T. W. Greene, 0. G. Wuts, Protective Groups in Organic Synthesis. Third Edition, 1999, Chapter 4, pp. 293-368, John Wiley & Sons, Inc. and the like, or based on that procedure.

Step 10 of Method B is a step to react the ketone compound (15) obtained in Step 8 with the compound (2) or compound (3) in an inert solvent in the presence of acid, to prepare a compound having the general formula (I).

Here, this reaction can be conducted in accordance with a similar procedure to Step 1.

Step 10' of Method B is a step to react the dimethylketal compound (16) obtained in Step 9 with the compound (2) or compound (3) in an inert solvent in the presence of acid, to prepare a compound having the general formula (I).

Here, this reaction can be conducted in accordance with a similar procedure to Step 1'.

<Method C>

Step 11 of Method C is a step, in the case where R^5 of the cyclic ketal compound (14) obtained in Method A or the compound having the general formula (I) obtained in Method B is a hydrogen atom, to react it with R^5-L (17) in an inert solvent in the presence of base, to prepare a compound having the general formula (I) which is substituted with a desired R^5.

R^5 and L represent the same meanings as described above, and "leaving group" in the definition of L represents a group which leaves as a nucleophilic residue, and for example, halogen atoms such as a fluorine atom, chlorine atom, bromine atom and iodine atom; lower-alkane sulfonyloxy groups such as methanesulfonyloxy and ethanesulfonyloxy; halogeno lower alkanesulfonyloxy groups such as trifluoromethanesulfonyloxy and pentafluoroethanesulfonyloxy; arylsulfonyloxy groups such as benzenesulfonyloxy, p-toluenesulfonyloxy and p-nitrobenzenesulfonyloxy; can be mentioned. Preferably, it is a halogen atom, particularly preferably an iodine atom.

The inert solvent used is not particularly limited so long as it does not inhibit the reaction and dissolves the starting material to some degree, and includes, for example, ketones such as acetone, methyl ethyl ketone, methyl isobutyl ketone, isophorone and cyclohexanone; ethers such as diethyl ether, diisopropyl ether, tetrahydrofuran and dioxane; aprotic polar solvents such as dimethylformamide, dimethylacetamide and dimethyl sulfoxide; nitrites such as acetonitrile; esters such as methyl acetate and ethyl acetate; aromatic hydrocarbons such as benzene, toluene and xylene; aliphatic hydrocarbons such as pentane, hexane and heptane, preferably, ethers, ketones or aprotic polar solvents, and more preferably, tetrahydrofuran, acetone or dimethylformamide.

The base used includes alkali metal carbonates such as sodium carbonate, potassium carbonate and lithium carbonate; alkali metal hydrogen carbonates such as sodium hydrogen carbonate, potassium hydrogen carbonate and lithium hydrogen carbonate; organic bases such as alkali metal alkoxides such as sodium methoxide, sodium ethoxide, potassium methoxide, potassium ethoxide, potassium t-butoxide and lithium methoxide; N-methylmorpholine, triethylamine, tripropylamine, tributylamine, diisopropylethylamine, dicyclohexylamine, N-methylpiperidine, pyridine, 4-pyrrolidinopyridine, picoline, 4-(N,N-dimethylamino)pyridine, 2,6-di (t-butyl)-4-methylpyridine, quinoline, N,N-dimethylaniline, N,N-diethylaniline, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,4-diazabicyclo[2.2.2]octane (DABCO) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), preferably alkali metal carbonates, and more preferably potassium carbonate.

Reaction temperature varies depending on the starting compound and reaction reagent, and the reaction is conducted from −78° C. to 150° C., preferably from −20° C. to 100° C.

Reaction time varies depending on the reaction temperature, starting compound, reaction reagent or the type of solvent used, and it is generally in the range from 1 minute to 24 hours, preferably from 10 minutes to 5 hours.

After each of the aforementioned reactions is completed, the desired compound is collected from the reaction mixture in accordance with general procedures.

For example, the reaction mixture is neutralized as needed, and after filtration to remove insoluble matters in the case where insoluble matters exist, the reaction solution is extracted with an organic solvent such as ethyl acetate, which does not blend with water. Then after washing the reaction solution with water and the like, the organic layer containing the desired compound is separated and dried over anhydrous magnesium sulfate and the like, and then the solvent is evaporated to give the desired compound.

The obtained desired compound may, if necessary, be separated and purified by ordinary procedures such as recrystallization and reprecipitation, or by a procedure generally used for separation and purification of organic compounds such as appropriately combining an adsorption column chromatography method which uses silica gel, alumina or florisil of magnesium-silica type as a support; a method using a synthetic adsorbent agent such as distribution column chromatography which uses Sephadex LH-20 (produced by Pharmacia), Amberlite XAD-11 (produced by Rohm and Haas) or Diaion HP-20 (produced by Mitsubishi Chemical Corporation) as a support, a method using ion exchange chromatography, or normal phase or reverse phase column chromatography by silica gel or alkylated silica gel (preferably high performance liquid chromatography) and eluting with an appropriate eluent.

The starting compounds such as (1), (2), (3), (5), (6), (9), (13) and (17) as reactive substances of the present invention are publicly known or can easily be prepared in accordance with publicly known procedures.

The compound having the general formula (I) according to the present invention or pharmacologically acceptable salts thereof possesses excellent activity to suppress intracellular signal transduction or cell activation in various cells such as monocytes, macrophages and vascular endothelial cells, the intracellular signal transduction and cell activation being induced by endotoxin, and to suppress various cell responses induced by the intracellular signal transduction and cell activation such as an excess generation of inflammatory mediators such as TNF-α. Therefore, it is useful as a medicament, especially as a prophylactic and/or therapeutic agent for various diseases which are associated with intracellular signal transduction or cell activation induced by endotoxin, and with various cell responses (for example, excess generation of

inflammatory mediators such as TNF-α) which are induced by the intracellular signal transduction and cell activation. As for such medicament, a prophylactic and/or therapeutic agent for ischemic brain disorder, arteriosclerosis, poor prognosis after coronary angioplasty, heart failure, diabetes, diabetic complication, joint inflammation, osteoporosis, osteopenia, sepsis, autoimmune disease, tissue disorder and rejection after organ transplantation, bacterial infection, virus infection, gastritis, pancreatitis, nephritis, pneumonia, hepatitis or leukemia can be mentioned.

In the case where the compound having the general formula (I) according to the present invention or the pharmacologically acceptable salts thereof is used as a prophylactic agent or a therapeutic agent for the aforementioned diseases, it can be mixed with excipients, diluents and the like that are themselves pharmacologically acceptable, and administered orally as a tablet, capsule, granules, powder or syrup, or administrated parenterally as an injection for subcutaneous injection, intramuscular injection or intravenous injection or as a suppository.

These pharmaceutical preparations are prepared in accordance with known processes by using additives including excipients (for example, organic excipients such as sugar derivatives, e.g. lactose, sucrose, glucose, mannitol or sorbitol; starch derivatives, e.g. corn starch, potato starch, α-starch or dextrin; cellulose derivatives, e.g. crystalline cellulose; gum arabic; dextran; or pullulan, and inorganic excipients such as silicate derivatives, e.g. light silicic anhydride, synthetic aluminum silicate, calcium silicate, metamagnesium aluminate; phosphates, e.g. calcium hydrogenphosphate; carbonates, e.g. calcium carbonate; salts of sulfuric acid such as calcium sulfate, can be mentioned), lubricants (for example, stearic acid, stearic acid metal salts such as calcium stearate or magnesium stearate; talc; colloid silica; waxes such as bees wax or spermaceti, boric acid; adipic acid; sulfates such as sodium sulfate; glycol; fumaric acid; sodium benzoate; DL leucine; lauryl sulfates such as sodium lauryl sulfate or magnesium lauryl sulfate; silicic acids such as silicic anhydride or silicate hydrate; and the aforementioned starch derivatives can be mentioned), binders (for example, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, polyvinylpyrrolidone, macrogol and compounds similar to the aforementioned excipient can be mentioned), disintegrants (for example, cellulose derivatives such as low-substituted hydroxypropyl cellulose, carboxymethyl cellulose, calcium carboxymethyl cellulose or internally crosslinked sodium carboxymethyl cellulose; or chemically modified starches or celluloses such as carboxymethyl starch, sodium carboxymethyl starch or crosslinked polyvinylpyrrolidone can be mentioned), emulsifiers (for example, colloidal clays such as bentonite or bee gum; metal hydroxides such as magnesium hydroxide or aluminum hydroxide; anionic surfactants such as sodium lauryl sulfate or calcium stearate; cationic surfactants such as benzalkonium chloride; and nonionic surfactants such as polyoxyethylene alkyl ether, polyoxyethylene sorbitan fatty acid ester or sucrose fatty acid ester), stabilizers (for example, paraoxybenzoic acid esters such as methyl paraben or propyl paraben; alcohols such as chlorobutanol, benzyl alcohol or phenyl ethyl alcohol, benzalkonium chloride; phenols such as phenol or cresol; thimerosal; dehydroacetic acid; and sorbic acid can be mentioned) and corrigents (for example, commonly used sweeteners, acidifiers or fragrances can be mentioned) or diluents.

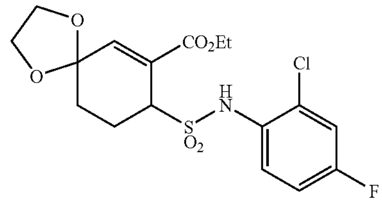
The amount of dosage varies according to symptoms and age, and it is desirable that the compound of the present invention is administered orally or parenterally to an adult human within a lower limit of 0.01 mg/kg (preferably 0.10 mg/kg) and an upper limit of 1000 mg/kg (preferably 100 mg/kg) per day, once a day or several times in parts depending on the symptoms.

EXAMPLES

Hereinafter, the present invention will be described in detail with reference to Examples and Test Examples, however, the scope of the present invention is not limited to these.

Example 1

Ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-364



(1a) Ethyl 8-acetylsulfanyl-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate

19.97 g (55.4 mmol) of ethyl 8-trifluoromethanesulfonyloxy-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate [compound described as compound 6 in Tetrahedron Letter, Vol. 39, pp. 6139-6142 (1998)] was dissolved in 200 ml of dimethylformamide, and 9.50 g (83.1 mmol) of potassium thioacetate was added thereto with stirring under ice-cooling, followed by stirring at room temperature for 91 hours. To the reaction solution was added ice water and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=17:3) to give 7.15 g of the title compound as a pale brown oil (yield: 45%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 4.20 (2H, q, 7 Hz), 4.04-3.96 (4H, m), 2.73-2.66 (4H, m), 2.34 (3H, s), 1.87 (2H, t, J=6 Hz), 1.28 (3H, t, J=7 Hz).

(1b) Ethyl 8-mercapto-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate

7.14 g (24.9 mmol) of ethyl 8-acetylsulfanyl-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate obtained in (1a) was dissolved in 145 ml of methanol, and 2.58 g (18.7 mmol) of potassium carbonate was added thereto with stirring under ice-cooling, followed by stirring at the same temperature for 1 hour and then at room temperature for 1 hour. The reaction solution was made acidic by addition of 1N hydrochloric acid and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=9:1) to give 5.63 g of the title compound as a pale yellow oil (yield: 92%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 4.32 (1H, s), 4.21 (2H, q, 7 Hz), 4.04-3.95 (4H, m), 2.72-2.67 (2H, m), 2.59-2.57 (2H, m), 1.82 (2H, t, J=7 Hz), 1.30 (3H, t, J=7 Hz).

(1c) Ethyl 8-chlorosulfonyl-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate

To a saturated solution prepared by blowing chlorine gas into 80 ml of solution mixture of acetonitrile-water (1:1) for 20 minutes was added a solution of 5.00 g (20.5 mmol) of ethyl 8-mercapto-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate obtained in (1b) in 10 ml of acetonitrile with stirring under ice-cooling. Chlorine gas was further blown into the reaction solution for 10 minutes at the same temperature. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=2:1) to give 5.83 g of the title compound as a colorless oil (yield: 92%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 4.30 (2H, q, 7 Hz), 4.05-3.98 (4H, m), 2.91-2.86 (2H, m), 2.71-2.69 (2H, m), 1.93 (2H, t, J=7 Hz), 1.34 (3H, t, J=7 Hz).

(1d) Ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate

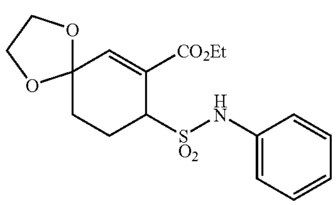
To a solution of 197 mg (1.35 mmol) of 2-chloro-4-fluoroaniline and 0.20 ml (1.42 mmol) of triethylamine in 5 ml of ethyl acetate was added dropwise a solution of 400 mg (1.29 mmol) of ethyl 8-chlorosulfonyl-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate obtained in (1c) in 3 ml of ethyl acetate with stirring under ice-cooling, followed by stirring at room temperature for 48 hours. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=3:1), and the resulting solid was further washed with a mixed solution of hexane-isopropyl ether (1:1) to give 325 mg of the title compound as a white powder (yield: 60%).

Melting point 117-119° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.67 (1H, dd, J=9 Hz, 5 Hz), 7.16 (1H, dd, J=8 Hz, 3 Hz), 7.05-6.98 (2H, m), 6.83 (1H, s), 4.43-4.41 (1H, m), 4.26-4.01 (5H, m), 3.95-3.88 (1H, m), 2.56-2.45 (2H, m), 2.24-2.11 (1H, m), 1.88-1.80 (1H, m), 1.27 (3H, t, J=7 Hz).

Example 2

Ethyl 8-(N-phenylsulfamoyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-12)

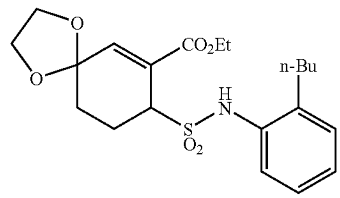


Following the process described in Example (1d), aniline was used in place of 2-chloro-4-fluoroaniline to give the title compound as an amorphous substance (yield: 81%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.37-7.31 (4H, m), 7.21-7.15 (1H, m), 6.95 (1H, s), 6.85-6.87 (1H, m), 4.30-4.20 (3H, m), 4.13-4.01 (3H, m), 3.94-3.88 (1H, m), 2.48-2.41 (1H, m), 2.31 (1H, td, J=14 Hz, 3 Hz), 2.10-2.00 (1H, m), 1.86-1.80 (1H, m), 1.31 (3H, t, J=7 Hz).

Example 3

Ethyl 8-[N-(2-butylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (exemplified compound No. 1-540)

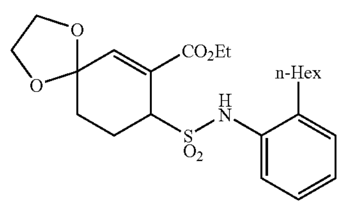


Following the process described in Example (1d), 2-butylaniline was used in place of 2-chloro-4-fluoroaniline to give the title compound as a colorless oil (56% yield).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.55-7.52 (1H, m), 7.22-7.17 (2H, m), 7.13-7.08 (1H, m), 6.85-6.84 (1H, m), 6.63 (1H, s), 4.47-4.44 (1H, m), 4.25-4.02 (5H, m), 3.95-3.89 (1H, m), 2.71-2.62 (2H, m), 2.54-2.38 (2H, m), 2.19-2.09 (1H, m), 1.86-1.81 (1H, m), 1.62-1.53 (2H, m), 1.45-1.34 (2H, m), 1.26 (3H, t, J=7 Hz), 0.95 (3H, t, J=7 Hz).

Example 4

Ethyl 8-[N-(2-hexylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-716)

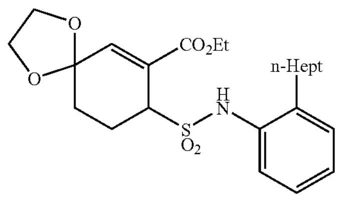


Following the process described in Example (1d), 2-hexylaniline was used in place of 2-chloro-4-fluoroaniline to give the title compound as a pale yellow oil (82% yield).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.55-7.52 (1H, m), 7.22-7.17 (2H, m), 7.13-7.08 (1H, m), 6.85-6.84 (1H, m), 6.63 (1H, s), 4.47-4.44 (1H, m), 4.25-4.02 (5H, m), 3.95-3.89 (1H, m), 2.70-2.61 (2H, m), 2.54-2.38 (2H, m), 2.19-2.09 (1H, m), 1.86-1.81 (1H, m), 1.64-1.54 (2H, m), 1.41-1.24 (6H, m), 1.26 (3H, t, J=7 Hz), 0.91-0.85 (3H, m).

Example 5

Ethyl 8-[N-(2-heptylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-892)

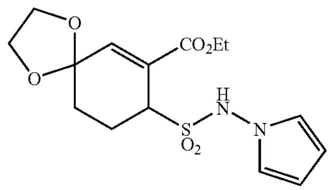


Following the process described in Example (1d), 2-heptylaniline was used in place of 2-chloro-4-fluoroaniline to give the title compound as a pale yellow oil (87% yield).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.55-7.52 (1H, m), 7.22-7.17 (2H, m), 7.13-7.08 (1H, m), 6.85-6.84 (1H, m), 6.63 (1H, s), 4.47-4.44 (1H, m), 4.25-4.02 (5H, m), 3.95-3.89 (1H, m), 2.69-2.61 (2H, m), 2.54-2.38 (2H, m), 2.19-2.09 (1H, m), 1.86-1.81 (1H, m), 1.64-1.54 (2H, m), 1.42-1.23 (8H, m), 1.26 (3H, t, J=7 Hz), 0.88 (3H, t, J=7 Hz).

Example 6

Ethyl 8-[N-(1H-pyrrol-1-yl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1062)



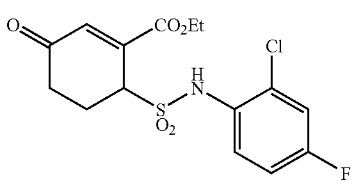
Following the process described in Example (id), 1H-pyrrol-1-ylamine was used in place of 2-chloro-4-fluoroaniline to give the title compound as a white powder (yield: 33%).

Melting point: 115-117° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 8.05 (1H, s), 6.99 (2H, t, J=2 Hz), 6.94 (1H, s), 6.17 (2H, t, J=2 Hz), 4.55-4.51 (1H, m), 4.30 (2H, q, J=7 Hz), 4.14-4.03 (3H, m), 3.98-3.89 (1H, m), 2.51-2.44 (1H, m), 2.26-2.05 (2H, m), 1.89-1.83 (1H, m), 1.35 (3H, t, J=7 Hz).

Example 7

Ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3-oxo-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-353)



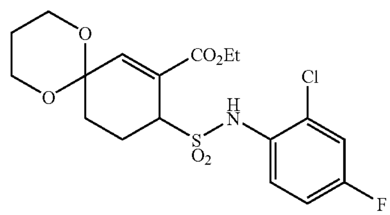
To 2.55 g (6.07 mmol) of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 1 was added 100 ml of a mixed solution of 1N hydrochloric acid-tetrahydrofuran (1:1), and the reaction solution was stirred at room temperature for 64 hours. Tetrahydrofuran was distilled off under reduced pressure, the residue was extracted by addition of ethyl acetate, and the organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=4:1), to give 2.19 g of the title compound as a pale brown powder (yield: 96%).

Melting point: 128-130° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.69 (1H, dd, J=9 Hz, 5 Hz), 7.20 (1H, dd, J=8 Hz, 3 Hz), 7.09-7.03 (1H, m), 6.91 (2H, s), 4.68 (1H, dd, J=5 Hz, 2 Hz), 4.28-4.18 (2H, m), 3.21-3.09 (1H, m), 2.80-2.72 (1H, m), 2.57-2.49 (1H, m), 2.44-2.31 (1H, m), 1.28 (3H, t, J=7 Hz).

Example 8

Ethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,5-dioxaspiro[5.5]undec-7-ene-8-carboxylate (exemplified compound No. 1-365)



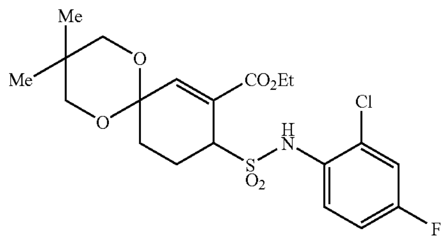
100 mg (0.27 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3-oxo-1-cyclohexene-1-carboxylate obtained in Example 7 was dissolved in 2 ml of toluene, and 0.04 ml (0.54 mmol) of propane-1,3-diol and 68 mg (0.27 mmol) of pyridinium p-toluenesulfonate were added thereto, followed by heating under reflux for 1 hour. After the reaction solution was cooled to room temperature, a saturated aqueous sodium hydrogencarbonate solution was added and extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane: ethyl acetate=2:1), and the resulting solid was further washed with hexane to give 60 mg of the title compound as a white powder (yield: 51%).

Melting point: 120-121° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.65 (1H, dd, J=9 Hz, 5 Hz), 7.36 (1H, s), 7.14 (1H, dd, J=8 Hz, 3 Hz), 7.01 (1H, dd, J=7 Hz, 2 Hz), 6.98 (1H, s), 4.45-4.39 (1H, m), 4.27-4.12 (2H, m), 4.11-3.84 (4H, m), 2.46-2.06 (4H, m), 1.92-1.67 (2H, m), 1.28 (3H, t, J=7 Hz).

Example 9

Ethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-dimethyl-1,5-dioxaspiro[5.5]undec-7-ene-8-carboxylate (Exemplified compound No. 1-426)

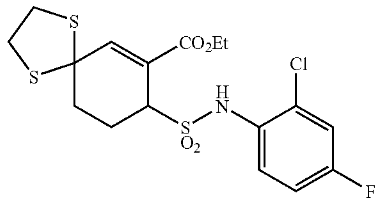


Following the process described in Example 8, 2,2-dimethylpropane-1,3-diol was used in place of propane-1,3-diol to give the title compound as a pale brown oil (yield: 64%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.64 (1H, dd, J=9 Hz, 5 Hz), 7.31 (1H, s), 7.13 (1H, dd, J=8 Hz, 3 Hz), 7.04-6.94 (2H, m), 4.45-4.39 (1H, m), 4.27-4.12 (2H, m), 3.69-3.46 (4H, m), 2.42-2.11 (4H, m), 1.28 (3H, t, J=7 Hz), 1.03 (3H, s), 0.97 (3H, s).

Example 10

Ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dithiaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-367)



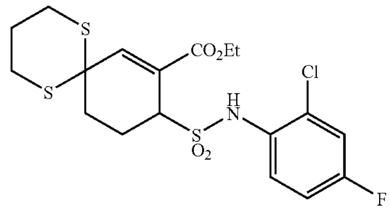
100 mg (0.27 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3-oxo-1-cyclohexene-1-carboxylate obtained in Example 7 was dissolved in 1 ml of dichloromethane and 0.034 ml (0.405 mmol) of ethane-1,2-dithiol and 0.025 ml (0.203 mmol) of boron trifluoride diethyl etherate were added thereto with stirring under ice-cooling, followed by stirring at room temperature for 1 hour. To the reaction solution was added a 1N aqueous sodium hydroxide solution and the mixture was extracted with diethyl ether. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The resulting solid was washed with diethyl ether and then with hexane to give 325 mg of the title compound as a white powder (76% yield).

Melting point: 160-161° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.65 (1H, dd, J=9 Hz, 5 Hz), 7.14 (1H, dd, J=8 Hz, 3 Hz), 7.10 (1H, s), 7.04-6.96 (2H, m), 4.40 (1H, d, J=5 Hz), 4.25-4.10 (2H, m), 3.52-3.26 (4H, m), 2.82-2.72 (1H, m), 2.58-2.50 (1H, m), 2.33-2.24 (1H, m), 2.11-1.99 (1H, m), 1.27 (3H, t, J=7 Hz).

Example 11

Ethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,5-dithiaspiro[5.5]undec-7-ene-8-carboxylate (Exemplified compound No. 1-368)

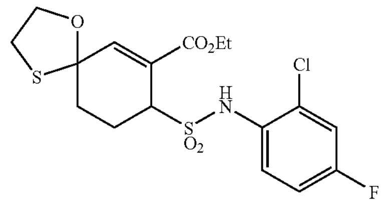


Following the process described in Example 10, propane-1,3-dithiol was used in place of ethane-1,2-dithiol to give the title compound as an amorphous substance (72% yield).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.65 (1H, dd, J=9 Hz, 5 Hz), 7.40 (1H, s), 7.14 (1H, dd, J=8 Hz, 3 Hz), 7.03-6.96 (1H, m), 6.94 (1H, s), 4.51 (1H, d, J=5 Hz), 4.24-4.11 (2H, m), 3.17-3.07 (1H, m), 2.98-2.77 (3H, m), 2.61-2.51 (1H, m), 2.47-2.38 (1H, m), 2.36-2.27 (1H, m), 2.25-2.13 (1H, m), 2.12-1.95 (2H, m), 1.27 (3H, t, J=7 Hz).

Example 12

Ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1-oxa-4-thiaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-371)



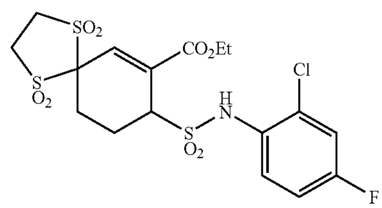
Following the process described in Example 10, 2-mercapteothanol was used in place of ethane-1,2-dithiol to give the title compound as a white powder (61% yield).

Melting point: 133-134° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.65 (1H, dd, J=9 Hz, 5 Hz), 7.14 (1H, dd, J=8 Hz, 3 Hz), 7.06 (0.4H, s), 7.04-6.96 (2.6H, m), 4.46 (0.4H, dd, J=5 Hz, 3 Hz), 4.39-4.01 (4.6H, m), 3.23-3.06 (2H, m), 2.77-2.51 (1.6H, m), 2.45-2.36 (0.4H, m), 2.20-2.00 (2H, m), 1.27 (3H, t, J=7 Hz).

Example 13

Ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,1,4,4-tetraoxo-1λ^6,4λ^6-dithiaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-369)



80 mg (0.18 mmol) of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dithiaspiro[4.5]dec-6-ene-7-carboxylate

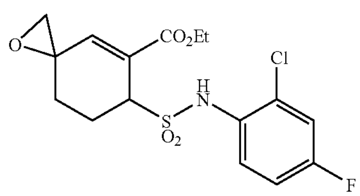
obtained in Example 10 was dissolved in 2 ml of dichloromethane, 91 mg (1.08 mmol) of sodium hydrogencarbonate was added thereto and subsequently 239 mg (0.90 mmol) of m-chloroperbenzoic acid (65%) was added with stirring under ice-cooling, followed by stirring at room temperature for 5 hours. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel thin layer chromatography (solvent; hexane:ethyl acetate=1:1) to give 42 mg of the title compound as a white powder (yield: 45%).

Melting point: 88-90° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.65 (1H, dd, J=9 Hz, 5 Hz), 7.15 (1H, dd, J=8 Hz, 3 Hz), 7.06-6.98 (2H, m), 6.92 (1H, s), 4.57 (1H, d, J=5 Hz), 4.26-4.16 (2H, m), 3.79-3.60 (4H, m), 3.14-2.98 (1H, m), 2.69-2.60 (1H, m), 2.45-2.36 (1H, m), 2.29-2.16 (1H, m), 1.28 (3H, t, J=7 Hz).

Example 14

Ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1-oxaspiro[2.5]oct-4-ene-5-carboxylate (Exemplified compound No. 1-360)

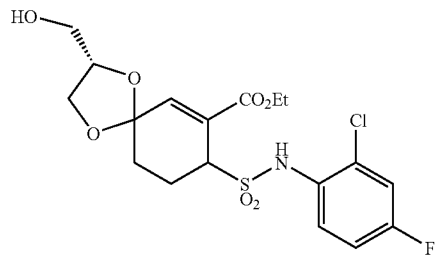


50 mg (0.133 mmol) of ethyl 6-[1-(2-chloro-4-fluorophenyl)sulfamoyl]-3-oxo-1-cyclohexene-1-carboxylate obtained in Example 7 and 0.01 ml (0.146 mmol) of dibromomethane were dissolved in 1 ml of tetrahydrofuran, and 0.18 ml (0.279 mmol) of n-butyllithium/hexane solution (1.58 M) was added dropwise thereto at −78° C., followed by stirring at room temperature for 4 hours. After the reaction solution was cooled with ice, a saturated aqueous ammonium chloride solution was added and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel thin layer chromatography (solvent; hexane:ethyl acetate=2:1) to give 7 mg of the title compound as a yellow oil (yield: 14%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.68 (1H, dd, J=9 Hz, 5 Hz), 7.15 (1H, dd, J=8 Hz, 3 Hz), 7.07-6.91 (2H, m), 6.60 (1H, s), 4.50 (1H, d, J=4 Hz), 4.27-4.06 (2H, m), 2.98-2.92 (1H, m), 2.91-2.88 (1H, m), 2.83-2.70 (1H, m), 2.68-2.59 (1H, m), 2.21-2.07 (2H, m), 1.25 (3H, t, J=7 Hz).

Example 15

Ethyl (2S)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-hydroxymethyl-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (exemplified compound No. 1-378)



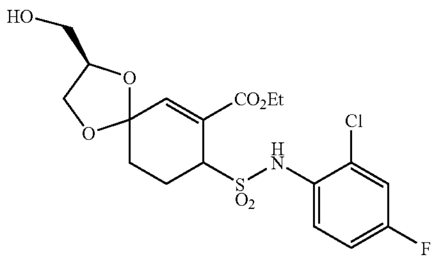
100 mg (0.27 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3-oxo-1-cyclohexene-1-carboxylate obtained in Example 7 and 69 mg (0.35 mmol) of (R)-2,3-dihydroxypropyl benzoate were dissolved in 2 ml of dichloromethane and 0.19 ml (1.05 mmol) of isopropoxytrimethylsilane and 2 μl (0.014 mmol) of trimethylsilyl trifluoromethanesulfonate were sequentially added thereto with stirring under ice-cooling, followed by stirring at the same temperature for 1 hour. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate 1:1), to give 121 mg of ethyl (2R)-2-benzoyloxymethyl-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate as a pale yellow oil (yield: 81%).

Subsequently, 121 mg (0.22 mmol) of this compound was dissolved in 2 ml of a mixture of methanol-tetrahydrofuran (1:1), and to the solution was added 0.5 ml (0.50 mmol) of 1N aqueous sodium hydroxide with stirring under ice-cooling, followed by stirring at the same temperature for 30 minutes. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=1:1) to give 41 mg of the title compound as an amorphous substance (yield: 41%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.64 (1H, dd, J=9 Hz, 5 Hz), 7.14 (1H, dd, J=8 Hz, 3 Hz), 7.06-6.97 (2H, m), 6.89 (0.25H, s), 6.86 (0.25H, s), 6.80 (0.25H, s), 6.78 (0.25H, s), 4.43-4.31 (1.75H, m), 4.26-4.02 (3.25H, m), 3.95-3.87 (0.75H, m), 3.85-3.77 (1H, m), 3.75-3.69 (0.25H, m), 3.68-3.59 (1H, m), 2.65-2.38 (2H, m), 2.25-2.11 (1H, m), 2.11-2.05 (0.25H, m), 2.03-1.97 (0.25H, m), 1.94-1.81 (1.5H, m), 1.26 (3H, t, J=7 Hz).

Example 16

Ethyl (2R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-hydroxymethyl-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-378)



(16a) Ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-dimethoxy-1-cyclohexene-1-carboxylate

6.1 g (16.2 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3-oxo-1-cyclohexene-1-carboxylate obtained in Example 7 was dissolved in 120 ml of methanol and 4.1 g (16.2 mmol) of pyridinium p-toluenesulfonate and 8.86 ml (81.0 mmol) of trimethoxymethane were sequentially added thereto with stirring under ice-cooling, followed by stirring overnight at room temperature. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=2:1) to give 6.0 g of the title compound as a white powder (yield: 88%).

Melting point: 97-98° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.65 (1H, dd, J=9 Hz, 5 Hz), 7.14 (1H, dd, J=8 Hz, 3 Hz), 7.07-6.97 (3H, m), 4.41 (1H, d, J=4 Hz), 4.28-4.12 (2H, m), 3.29 (3H, s), 3.23 (3H, s), 2.47-2.38 (1H, m), 2.31-2.21 (1H, m), 2.18-2.06 (1H, m), 2.01-1.93 (1H, m), 1.28 (3H, t, J=7 Hz).

(16b) Ethyl (2R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-hydroxymethyl-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate

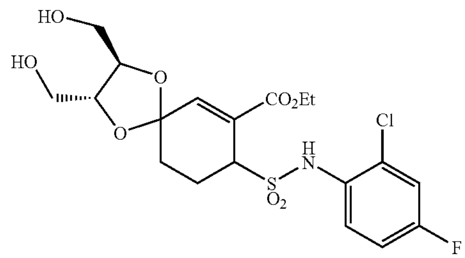
342 mg (0.81 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-dimethoxy-1-cyclohexen-1-carboxylate obtained in (16a) and 206 mg (1.05 mmol) of (S)-2,3-dihydroxypropyl benzoate were dissolved in 7 ml of dichloromethane, and 0.56 ml (3.15 mmol) of isopropoxytrimethylsilane and 7 μl (0.041 mmol) of trimethylsilyl trifluoromethanesulfonate were added thereto sequentially with stirring under ice-cooling, followed by stirring for 1 hour at the same temperature. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=1:1), to give 410 mg of ethyl (2S)-2-benzoyloxymethyl-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate as a colorless oil (yield: 91%).

Subsequently, 410 mg (0.74 mmol) of this compound was dissolved in 10 ml of a mixture of methanol-tetrahydrofuran (1:1) and 3 ml (3.0 mmol) of 1N aqueous sodium hydroxide was added thereto, followed by stirring for 15 minutes at room temperature. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=1:1) to give 293 mg of the title compound as an amorphous substance (yield: 88%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.64 (1H, dd, J=9 Hz, 5 Hz), 7.14 (1H, dd, J=8 Hz, 3 Hz), 7.04-6.95 (2H, m), 6.89 (0.42H, s), 6.86 (0.02H, s), 6.80 (0.02H, s), 6.78 (0.42H, s), 4.43-4.31 (1.5H, m), 4.26-4.02 (2.5H, m), 3.96-3.89 (1H, m), 3.83-3.77 (0.5H, m), 3.75-3.69 (0.5H, m), 3.68-3.59 (1H, m), 2.65-2.41 (2H, m), 2.25-2.10 (1H, m), 1.93-1.82 (1H, m), 1.77-1.67 (0.5H, br. s), 1.58 (0.5H, br. s), 1.26 (3H, t, J=7 Hz).

Example 17

Ethyl (2R,3R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-382)



Following the process described in Example (16b), 1,4-di-O-benzoyl-D-threitol was used in place of (S)-2,3-dihydroxypropyl benzoate to give the title compound as an amorphous substance (yield: 44%).

<Alternative Procedure>

(17a) Ethyl (2R,3R)-2,3-bis(benzoyloxymethyl)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate

1.46 g (3.08 mmol) of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-D-threitol obtained in Reference Example 18 was suspended in 2 ml of acetonitrile, and 0.04 ml (0.24 mmol) of trimethylsilyl trifluoromethanesulfonate and a solution of 1.00 g (2.37 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-dimethoxy-1-cyclohexene-1-carboxylate obtained in Example (16a) in 5 ml of acetonitrile were sequentially added thereto with stirring under ice-cooling, followed by stirring for 1 hour at the same temperature. The reaction solution was concentrated under reduced pressure, and the residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=2:1) to give 1.50 g of the title compound as a pale yellow powder (yield: 92%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 8.10-8.04 (4H, m), 7.68-7.57 (3H, m), 7.49-7.44 (4H, m), 7.16 (1H, dt, J=8.0 Hz, 2.6 Hz), 7.05-7.00 (2H, m), 6.87 (1H, d, J=14.0 Hz), 4.66-4.07 (9H, m), 2.63-2.44 (2H, m), 2.25-2.19 (1H, m), 1.94 (1H, t, J=15.2 Hz), 1.19 (3H, t, J=7.0 Hz).

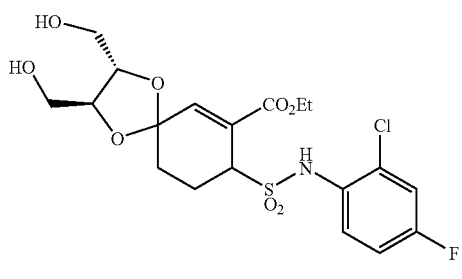
(17b) Ethyl (2R,3R)-8-[N-(2-chloro-4-fluorophenyl) sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro [4.5]dec-6-ene-7-carboxylate

1.50 g (2.18 mmol) of ethyl (2R,3R)-2,3-bis(benzoyloxymethyl)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in (17a) was dissolved in 10 ml of a mixture of methanol-tetrahydrofuran (4:1), and 10 ml (10.0 mmol) of 1N aqueous sodium hydroxide was added thereto with stirring under ice-cooling, followed by stirring for 15 minutes at the same temperature. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=1:1) to give 900 mg of the title compound as a white amorphous substance (yield: 86%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.69-7.64 (1H, m), 7.16 (1H, dd, J=8 Hz, 3 Hz), 7.05-6.99 (2H, m), 6.91-6.90 (0.5H, m), 6.85-6.84 (0.5H, m), 4.43-4.41 (1H, m), 4.27-4.09 (3.5H, m), 4.05-4.01 (0.5H, m), 3.93-3.81 (2H, m), 3.75-3.69 (2H, m), 2.59-2.45 (2H, m), 2.23-1.50 (4H, m), 1.29-1.24 (3H, m).

Example 18

Ethyl (2S,3S)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5] dec-6-ene-7-carboxylate (Exemplified compound No. 1-382)



Following the process described in Example (16b), 1,4-di-O-benzoyl-L-threitol was used in place of (S)-2,3-dihydroxypropyl benzoate to give the title compound as an amorphous substance (34% yield).

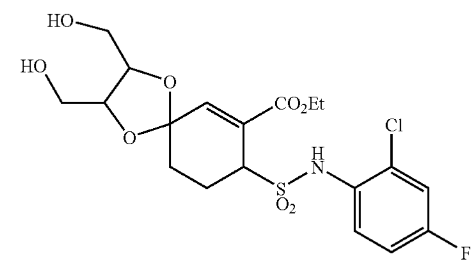
<Alternative Procedure>

Following the process described in Example 17 (alternative procedure), 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-L-threitol obtained in Reference Example 19 was used in place of 1,4-di-o-benzoyl-2,3-di-o-trimethylsilyl-D-threitol to give the title compound as an amorphous substance (yield: 73%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.69-7.64 (1H, m), 7.16 (1H, dd, J=8 Hz, 3 Hz), 7.05-6.99 (2H, m), 6.91-6.90 (0.5H, m), 6.85-6.84 (0.5H, m), 4.43-4.41 (1H, m) 4.27-4.09 (3.5H, m), 4.05-4.01 (0.5H, m), 3.93-3.81 (2H, m), 3.75-3.69 (2H, m), 2.59-2.45 (2H, m), 2.23-1.50 (4H, m), 1.29-1.24 (3H, m).

Example 19

Ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-meso-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5] dec-6-ene-7-carboxylate (Exemplified compound No. 1-382)



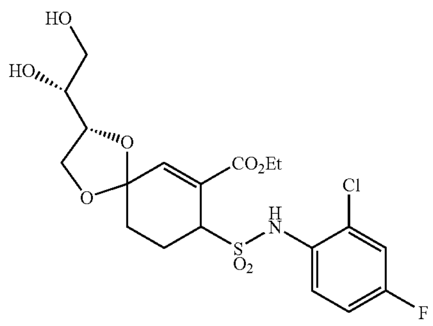
200 mg (0.47 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-dimethoxy-1-cyclohexene-1-carboxylate obtained in Example (16a) and 290 mg (0.61 mmol) of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-meso-erythritol obtained in Reference Example 1 were dissolved in 4 ml of dichloromethane and 4 μl (0.024 mmol) of trimethylsilyl trifluoromethanesulfonate was added thereto with stirring under ice-cooling, followed by stirring for 1 hour at the same temperature. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=2:1) to give 171 mg of ethyl meso-2,3-bis[(benzoyloxy)methyl]-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate as an amorphous substance (yield: 53%).

Subsequently, 170 mg (0.25 mmol) of this compound was dissolved in 10 ml of a mixture of methanol-tetrahydrofuran (1:1), and 3 ml (3.0 mmol) of 1N aqueous sodium hydroxide was added thereto with stirring under ice-cooling, followed by stirring for 15 minutes at the same temperature. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane: ethyl acetate=1:3) to give 105 mg of the title compound as an amorphous substance (yield: 89%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.64 (1H, dd, J=9 Hz, 5 Hz), 7.15 (1H, dd, J=8 Hz, 3 Hz), 7.04-6.95 (2H, m), 6.93 (0.4H, s), 6.72 (0.6H, s), 4.49-4.33 (2.4H, m), 4.32-4.26 (0.6H, m), 4.25-4.07 (2H, m), 3.93-3.70 (4H, m), 2.69-2.58 (0.4H, m), 2.58-2.35 (3.6H, m), 2.24-2.09 (1H, m), 1.99-1.91 (0.6H, m), 1.90-1.83 (0.4H, m), 1.27 (3H, t, J=7 Hz).

Example 20

Ethyl (2R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-((1R)-1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-390)



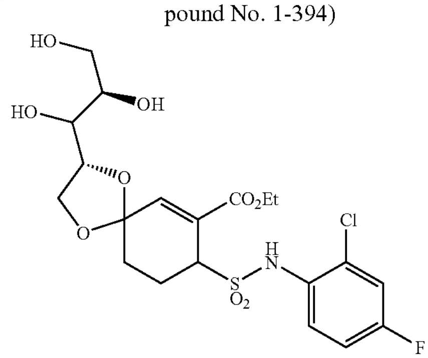
300 mg (0.71 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-dimethoxy-1-cyclohexene-1-carboxylate obtained in Example (16a) and 436 mg (1.42 mmol) of (4R,5R)-2,2-dimethyl-4,5-bis[(trimethylsilyl)oxy]methyl[1.3]dioxolane were dissolved in 12 ml of dichloromethane and 26 μl (0.142 mmol) of trimethylsilyl trifluoromethanesulfonate was added thereto with stirring under ice-cooling, followed by stirring for 90 hours at room temperature. Saturated aqueous sodium hydrogencarbonate was added to the reaction solution and the mixture was extracted with dichloromethane. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=4:1) to give 90 mg of ethyl (2R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-((4R)-2,2-dimethyl[1.3]dioxolan-4-yl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate as an amorphous substance (yield: 24%).

Subsequently, to 85 mg (0.163 mmol) of this compound was added 4 ml of a mixture of acetic acid-water (1:1), followed by stirring overnight at room temperature. The reaction solution was neutralized with addition of saturated aqueous sodium hydrogencarbonate, and the mixture was then extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; ethyl acetate alone) to give 46 mg of the title compound as an amorphous substance (yield: 59%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.69-7.64 (1H, m), 7.19-7.15 (1H, m), 7.06-6.98 (2H, m), 6.89-6.80 (1H, m), 4.43-4.41 (1H, m), 4.38-4.08 (4H, m), 4.03-3.95 (0.7H, m), 3.86 (0.3H, t, J=8 Hz), 3.77-3.63 (3H, m), 2.67-2.37 (3H, m), 2.22-1.84 (3H, m), 1.30-1.25 (3H, m).

Example 21

Ethyl (2R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-((2R)-1,2,3-trihydroxypropyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-394)

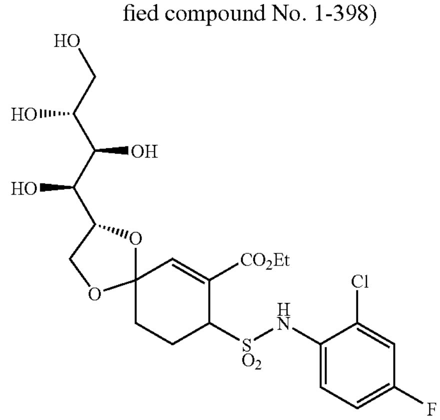


547 mg (1.07 mmol) of 1,3,4,5,7-penta-O-trimethylsilyl-D-arabitol obtained in Reference Example 2 was dissolved in 3 ml of nitromethane, to the resulting solution was added 13 μl (0.007 mmol) of trimethylsilyl trifluoromethanesulfonate and was then added 300 mg (0.71 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-dimethoxy-1-cyclohexene-1-carboxylate obtained in Example (16a) with stirring under ice-cooling, followed by stirring for 1 hour at the same temperature. A saturated aqueous sodium hydrogencarbonate was added to the reaction solution and the mixture was extracted with dichloromethane. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; ethyl acetate alone) to give 151 mg of the title compound as an amorphous substance (yield: 42%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.66 (1H, dd, J=9 Hz, 5 Hz), 7.19-7.15 (1H, m), 7.10-6.99 (2H, m), 6.86 (0.5H, s), 6.82-6.80 (0.5H, m), 4.42-4.39 (1H, m), 4.28-3.65 (9H, m), 3.20-1.40 (3H, br), 2.57-2.43 (2H, m), 2.23-2.09 (1H, m), 1.92-1.82 (1H, m), 1.29-1.25 (3H, m).

Example 22

Ethyl (2R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-((1S,2R,3R)-1,2,3,4-tetrahydroxybutyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-398)



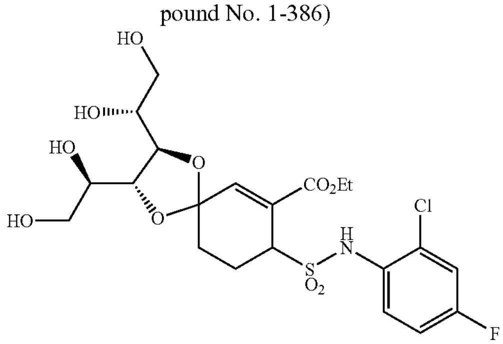
200 mg (0.47 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-dimethoxy-1-cyclohexene-1-carboxy-

late obtained in Example (16a) and 434 mg (0.71 mmol) of 1,2,3,4,5,6-hexa-O-trimethylsilyl-D-mannitol were dissolved in 4 ml of dichloromethane, to the resulting solution were added sequentially 0.12 ml (0.47 mmol) of isopropoxytrimethylsilane and 4 μl (0.024 mmol) of trimethylsilyl trifluoromethanesulfonate with stirring under ice-cooling, followed by stirring overnight at room temperature. Saturated aqueous sodium hydrogencarbonate was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; dichloromethane: methanol=10:1) to give 130 mg of the title compound as an amorphous substance (yield: 51%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.62 (1H, dd, J=9 Hz, 5 Hz), 7.22-7.12 (2H, m), 7.04-6.96 (1H, m), 6.88-6.84 (0.2H, m), 6.80-6.77 (0.4H, m), 6.76 (0.4H, s), 4.41-4.31 (1H, m), 4.25-4.03 (4H, m), 3.98-3.63 (6H, m), 2.54-2.41 (2H, m), 2.22-2.08 (1H, m), 1.92-1.81 (1H, m), 1.26 (3H, t, J=7 Hz).

Example 23

Ethyl (2R,3R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis((1R)-1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-386)



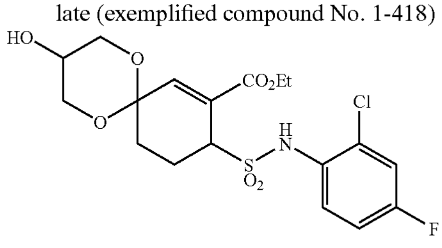
Following the process described in Example 19, 1,6-di-O-benzoyl-2,3,4,5-tetra-O-trimethylsilyl-D-mannitol obtained in Reference Example 3 was used in place of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-meso-erythritol to give the title compound as a white powder (yield: 11%).

Melting point: 55-56° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.65 (1H, dd, J=9 Hz, 5 Hz), 7.20-7.13 (2H, m), 7.06-7.00 (1H, m), 6.80 (0.5H, s), 6.78 (0.5H, s), 4.38 (1H, d, J=5 Hz), 4.26-4.00 (5H, m), 3.98-3.88 (1.5H, m), 3.87-3.65 (5.5H, m), 2.78-2.56 (2H, m), 2.55-2.40 (2H, m), 2.23-2.09 (1H, m), 1.92-1.80 (1H, m), 1.26 (3H, t, J=7 Hz).

Example 24

Ethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3-hydroxy-1,5-dioxaspiro[5.5]undec-7-ene-8-carboxylate (exemplified compound No. 1-418)

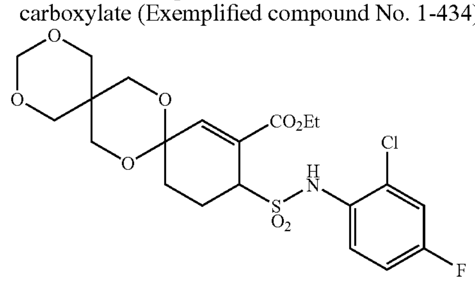


Following the process described in Example 19, 2-trimethylsilyloxy-1-trimethylsilyloxymethylethyl adamantan-1-carboxylate obtained in Reference Example 4 was used in place of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-meso-erythritol to give the title compound as an amorphous substance (yield: 17%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.69-7.64 (1H, m), 7.52-7.51 (0.5H, m), 7.18-7.15 (1H, m), 7.08-6.99 (2.5H, m), 4.45-4.42 (1H, m), 4.31-4.05 (4H, m), 3.88-3.74 (2H, m), 3.72-3.63 (1H, m), 2.78-2.52 (1H, br), 2.48-1.97 (4H, m), 1.31-1.26 (3H, m).

Example 25

Ethyl 12-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,4,8,5-tetraoxadispiro[5.2.5.2]hexadec-10-ene-11-carboxylate (Exemplified compound No. 1-434)



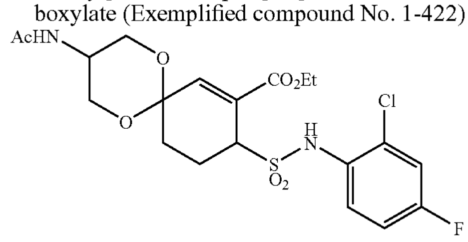
100 mg (0.266 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3-oxo-1-cyclohexene-1-carboxylate obtained in Example 7 and 156 mg (0.532 mmol) of 5,5-bis[(trimethylsilyl)oxy]methyl[1.3]dioxane were dissolved in 2 ml of dichloromethane and 10 μl (0.053 mmol) of trimethylsilyl trifluoromethanesulfonate was added thereto at −78° C., followed by stirring for 30 minutes at the same temperature and then for 2 hours at room temperature. Saturated aqueous sodium hydrogencarbonate was added to the reaction solution and the mixture was extracted with dichloromethane. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=2:1) and the resulting solid was further washed with isopropyl ether to give 49 mg of the title compound as a white powder (yield: 52%).

Melting point: 156-157° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.66 (1H, dd, J=9 Hz, 5 Hz), 7.17 (1H, dd, J=8 Hz, 3 Hz), 7.05-6.98 (2H, m), 4.83 (1H, d, J=6 Hz), 4.78 (1H, d, J=6 Hz), 4.44-4.42 (1H, m), 4.29-4.14 (2H, m), 3.87-3.70 (8H, m), 2.44-2.38 (1H, m), 2.32-2.24 (1H, m), 2.18-2.08 (2H, m), 1.28 (3H, t, J=7 Hz).

Example 26

Ethyl 3-acetylamino-9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,5-dioxaspiro[5.5]undec-7-ene-8-carboxylate (Exemplified compound No. 1-422)



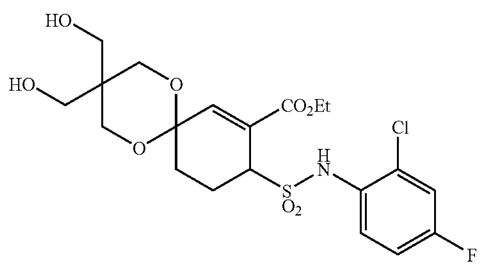
500 mg (1.19 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-dimethoxy-1-cyclohexene-1-carboxylate obtained in Example (16a) and 205 mg (1.54 mmol) of

N-(2-hydroxy-1-hydroxymethylethyl)acetamide were dissolved in 20 ml of dichloromethane, and 0.84 ml (4.74 mmol) of isopropoxytrimethylsilane and 43 μl (0.24 mmol) of trimethylsilyl trifluoromethanesulfonate were added sequentially with stirring under ice-cooling, followed by stirring for 30 minutes at the same temperature, and further for 66 hours at room temperature. Saturated aqueous sodium hydrogencarbonate was added to the reaction solution and the mixture was extracted with dichloromethane. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; ethyl acetate methanol=39:1) to give 288 mg of the title compound as an amorphous substance (yield: 50%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.66 (1H, dd, J=9 Hz, 5 Hz), 7.62-7.60 (0.5H, m), 7.17 (1H, dd, J=8 Hz, 3 Hz), 7.05-6.99 (2H, m), 6.93-6.91 (0.5H, m), 6.35 (1H, br.d, J=8 Hz), 4.46-4.42 (1H, m), 4.35-4.11 (4H, m), 4.03-3.95 (1H, m), 3.82-3.70 (2H, m), 2.60-2.55 (0.5H, m), 2.48-2.01 (3H, m), 2.06 (3H, s), 1.95-1.90 (0.5H, m), 1.30 (3H, t, J=7 Hz).

Example 27

Ethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-bis(hydroxymethyl)-1,5-dioxaspiro[5.5]undec-7-ene-8-carboxylate (Exemplified compound No. 1-430)

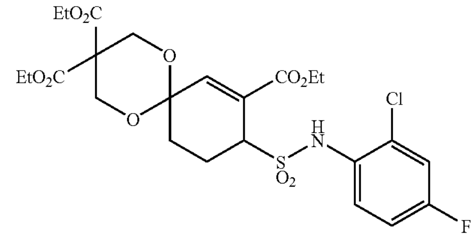


500 mg (1.19 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-dimethoxy-1-cyclohexene-1-carboxylate obtained in Example (16a) and 1.0 g (2.38 mmol) of 1,3-bis[(trimethylsilyl)oxy]-2,2-bis[(trimethylsilyl)oxy]methylpropane were dissolved in 10 ml dichloromethane and 10 μl (0.06 mmol) of trimethylsilyl trifluoromethanesulfonate was added thereto with stirring under ice-cooling, followed by stirring for 2 hours at the same temperature. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; ethyl acetate alone) to give 510 mg of the title compound as an amorphous substance (yield: 87%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.66 (1H, dd, J=9 Hz, 5 Hz), 7.28 (1H, s), 7.17 (1H, dd, J=8 Hz, 3 Hz), 7.11 (1H, s), 7.07-6.98 (1H, m), 4.42 (1H, d, J=4 Hz), 4.30-4.10 (2H, m), 3.92-3.68 (8H, m), 2.54-2.36 (3H, m), 2.34-2.23 (1H, m), 2.21-2.07 (2H, m), 1.28 (3H, t, J=7 Hz).

Example 28

Triethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,5-dioxaspiro[5.5]undec-7-ene-3,3,8-tricarboxylate (Exemplified compound No. 1-438)

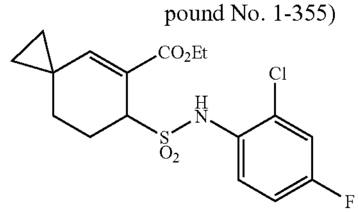


Following the process described in Example 27, diethyl 2,2-bis[(trimethylsilyl)oxy]methylmalonate obtained in Reference Example 5 was used in place of 1,3-bis[(trimethylsilyl)oxy]-2,2-bis[(trimethylsilyl)oxy]methylpropane to give the title compound as an amorphous substance (yield: 42%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.65 (1H, dd, J=9 Hz, 5 Hz), 7.23-7.21 (1H, m), 7.16 (1H, dd, J=8 Hz, 3 Hz), 7.04-6.99 (1H, m), 6.97 (1H, s), 4.43-4.36 (3H, m), 4.31-4.13 (8H, m), 2.44-2.37 (1H, m), 2.33-2.25 (1H, m), 2.19-2.06 (2H, m), 1.283 (3H, t, J=7 Hz), 1.280 (6H, t, J=7 Hz).

Example 29

Ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]spiro[2.5]oct-4-ene-5-carboxylate (Exemplified compound No. 1-355)



(29a) Ethyl 3-[1-(2-ethoxycarbonylethyl)cyclopropyl]propionate

24.5 ml (24.5 mmol) of 1.0 M diethyl zinc/hexane solution was added to 30 ml of dichloromethane, and then a solution of 1.89 ml (24.5 mmol) of trifluoroacetic acid in 10 ml of dichloromethane was added with stirring under ice-cooling. The reaction solution was stirred for 20 minutes at the same temperature, then a solution of 1.97 ml (24.5 mmol) of diiodomethane in 10 ml of dichloromethane was added and stirred for 20 minutes, and 1.40 g (6.13 mmol) of a solution of diethyl 4-methyleneheptanedicarboxylate (compound described in J.A.C.S. 107, 13, 3981-3997 (1985)) in 10 ml of dichloromethane was further added. After the reaction solution was stirred for 6 hours at room temperature, ice water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane: ethyl acetate=5:1) to give 1.48 g of the title compound as a brown oil (yield: 99%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 4.10 (2H, q, J=7 Hz), 3.37-2.31 (4H, m), 1.60-1.53 (4H, m), 1.25 (6H, t, J=7 Hz), 0.31 (4H, s).

(29b) Ethyl 6-hydroxyspiro[2.5]oct-5-ene-5-carboxylate

1.46 g (6.03 mmol) of ethyl 3-[1-(2-ethoxycarbonylethyl) cyclopropyl]propionate obtained in (29a) was dissolved in 60 ml of tetrahydrofuran and 1.35 g (12.1 mmol) of potassium t-butoxide was added thereto, followed by stirring for 1 hour at room temperature. The reaction solution was cooled with ice and made acidic by addition of 1N hydrochloric acid, and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; ethyl acetate alone) to give 1.05 g of the title compound as a yellow oil (yield: 89%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 12.23 (0.7H, s), 4.26-4.09 (2H, m), 3.50 (0.3H, dd, J=10 Hz, 6 Hz), 2.57-2.42 (0.7H, m), 2.36 (2H, t, J=6 Hz), 2.03-1.94 (0.3H, m), 1.66-1.52 (1H, m), 1.48 (2H, t, J=6 Hz), 1.28 (3H, J=7 Hz), 0.60-0.30 (4H, m).

(29c) Ethyl 6-trifluoromethanesulfonyloxyspiro[2.5]oct-5-ene-5-carboxylate

1.05 g (5.35 mmol) of ethyl 6-hydroxyspiro[2.5]oct-5-ene-5-carboxylate obtained in (29b) was dissolved in 30 ml of dichloromethane, and 0.99 ml (5.89 mmol) of diisopropylethylamine and 1.40 ml (8.03 mmol) of trifluoromethanesulfonic anhydride were added sequentially with stirring at −78° C. After the reaction solution was stirred for 3 hours at the same temperature, it was warmed to room temperature. The reaction solution was poured into saturated aqueous sodium hydrogencarbonate and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; ethyl acetate alone) to give 1.56 g of the title compound as a brown oil (yield: 89%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 4.26 (2H, q, J=7 Hz), 2.57-2.46 (2H, m), 2.35-2.29 (2H, m), 1.60-1.53 (2H, m), 1.32 (3H, t, J=7 Hz), 0.49-0.40 (4H, m).

(29d) Ethyl 6-mercaptospiro[2.5]oct-5-ene-5-carboxylate

Following the process described in Example (1a), ethyl 6-trifluoromethanesulfonyloxyspiro[2.5]oct-5-ene-5-carboxylate obtained in (29c) was used in place of ethyl 8-trifluoromethanesulfonyloxy-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate to give ethyl 6-acetylsulfanylspiro[2.5]oct-5-ene-5-carboxylate as a pale yellow oil (yield: 58%).

Subsequently, 700 mg (2.75 mmol) of this compound was dissolved in 14 ml of ethanol, and 2.75 ml (11 mmol) of 4N hydrogen chloride/dioxane solution was added thereto with stirring under ice-cooling, followed by stirring for 4 hours at room temperature. The reaction solution was concentrated under reduced pressure, and the residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=10:1), to give 300 mg of the title compound as a pale yellow oil (yield: 51%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 4.19 (2H, q, J=7 Hz), 4.12 (1H, s), 2.57 (2H, t, J=6 Hz), 2.22-2.18 (2H, m), 1.46 (2H, t, J=6 Hz), 1.29 (3H, t, J=7 Hz), 0.40-0.33 (4H, m).

(29e) Ethyl 6-(chlorosulfonyl)spiro[2.5]oct-5-ene-5-carboxylate

7 ml of acetic acid was added to 651 mg (4.23 mmol) of sodium perborate tetrahydrate, the mixture was heated to 50° C., and a solution of 300 mg (1.41 mmol) of ethyl 6-mercaptospiro[2.5]oct-5-ene-5-carboxylate obtained in (29d) in 3 ml of acetic acid was added thereto, followed by stirring for 2 hours at the same temperature and further for 3 hours at 80° C. The reaction solution was cooled to room temperature and concentrated under reduced pressure. 5 ml of thionyl chloride was added to the residue, and the mixture was heated under reflux for 2 hours. The reaction solution was cooled to room temperature again and concentrated under reduced pressure. Ice water was added to the residue and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=5:1 to give 195 mg of the title compound as a colorless oil (yield: 50%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 4.28 (2H, q, J=7 Hz), 2.77-2.69 (2H, m), 2.43-2.38 (2H, m), 1.62 (2H, t, J=6 Hz), 1.33 (3H, t, J=7 Hz), 0.52-0.46 (4H, m).

(29f) Ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]spiro[2.5]oct-4-ene-5-carboxylate

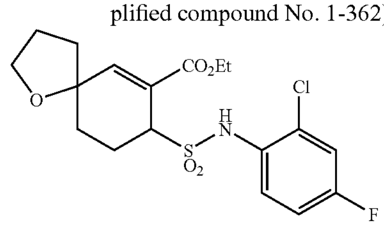
Following the process described in Example (1d), ethyl 6-(chlorosulfonyl)spiro[2.5]oct-5-ene-5-carboxylate obtained in (29e) was used in place of ethyl 8-chlorosulfonyl-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate to give the title compound as a white powder (yield: 17%).

Melting point: 125-126° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 7.69 (1H, dd, J=9 Hz, 5 Hz), 7.13 (1H, dd, J=8 Hz, 3 Hz), 7.03-6.96 (2H, m), 6.58 (1H, s), 4.53 (1H, d, J=5 Hz), 4.20-4.04 (2H, m), 2.62-2.50 (2H, m), 1.98-1.85 (1H, m), 1.23 (3H, t, J=7 Hz), 1.22-1.13 (1H, m), 1.09-0.99 (2H, m), 0.93-0.80 (2H, m).

Example 30

Ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1-oxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity diastereomer), (high polarity diastereomer) (Exemplified compound No. 1-362)



(30a) 7-(1,3-Dioxan-2-yl)-5-[2-(1,3-dioxan-2-yl)ethyl]heptane-1,5-diol

430 mg (5 mmol) of γ-butyrolactone was dissolved in 10 ml of tetrahydrofuran, and 22 ml (11 mmol) of 0.5 M (1,3-dioxan-2-ylethyl)magnesium bromide/tetrahydrofuran solution was added thereto with stirring under ice-cooling, fol-

lowed by stirring for 3 hours at 50° C. After the reaction solution was cooled with ice, saturated aqueous ammonium chloride was added and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; ethyl acetate: ethanol=10:1) to give 880 mg of the title compound as a colorless oil (yield: 55%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.51 (2H, t, J=5 Hz), 4.08 (4H, dd, J=10 Hz, 4 Hz), 3.79-3.70 (4H, m), 3.61 (2H, t, J=6 Hz), 2.13-2.00 (2H, m), 1.68-1.56 (12H, m), 1.55-1.49 (2H, m), 1.37-1.29 (2H, m).

(30b) 2-(2-{2-[2-(1,3-dioxan-2-yl)ethyl]tetrahydrofuran-2-yl}ethyl)-1,3-dioxane

2.60 g (8.17 mmol) of 7-(1,3-dioxan-2-yl)-5-[2-(1,3-dioxan-2-yl)ethyl]heptane-1,5-diol obtained in (30a) was dissolved in 45 ml of pyridine, and a solution of 1.64 g (8.58 mmol) of p-toluenesulfonyl chloride in 15 ml of pyridine was added thereto with stirring under ice-cooling, followed by stirring for 1 hour at the same temperature and further for 3 hours at room temperature. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=1:1) to give 1.31 g of the title compound as a colorless oil (yield: 53%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.50 (2H, t, J=5 Hz), 4.09 (2H, dd, J=11 Hz, 5 Hz), 3.83-3.68 (6H, m), 2.15-1.99 (2H, m), 1.92-1.82 (2H, m), 1.73-1.48 (12H, m), 1.38-1.29 (2H, m).

(30c) Ethyl 3-[2-(2-ethoxycarbonylethyl)tetrahydrofuran-2-yl]propionate

1.31 g (43.6 mmol) of 2-(2-{(2-[2-(1,3-dioxan-2-yl)ethyl] tetrahydrofuran-2-yl}ethyl)-1,3-dioxane obtained in (30b) was dissolved in 15 ml of acetone, and 16.3 ml (43.6 mmol) of Jones reagent was added thereto with stirring under ice-cooling, followed by stirring for 3 hours at room temperature. The reaction solution was cooled with ice, and then the reaction was terminated by addition of isopropyl alcohol. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was dissolved in 15 ml of ethanol, and 0.76 ml (10.5 mmol) of thionyl chloride was added, followed by stirring overnight at room temperature. The reaction solution was concentrated under reduced pressure, and the residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=1:1) to give 610 mg of the title compound as a yellow oil (yield: 51%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.13 (4H, q, J=7 Hz), 3.78 (2H, t, J=7 Hz), 2.37-2.31 (4H, m), 1.95-1.87 (2H, m), 1.86-1.79 (4H, m) 1.71 (2H, t, J=7 Hz), 1.26 (6H, t, J=7 Hz).

(30d) Ethyl 8-oxo-1-oxaspiro[4.5]decane-7-carboxylate

610 mg (2.24 mmol) of ethyl 3-[2-(2-ethoxycarbonylethyl) tetrahydrofuran-2-yl]propionate obtained in (30c) was dissolved in 18 ml of tetrahydrofuran, and 503 mg (4.48 mmol) of potassium t-butoxide was added thereto, followed by heating under reflux for 1 hour. After the reaction solution was cooled with ice, the reaction solution was made acidic by addition of 1N hydrochloric acid, and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=2:1) to give 340 mg of the title compound as a colorless oil (yield: 67%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

12.24 (1H, s), 4.26-4.12 (2H, m), 3.96-3.79 (2H, m), 2.63-2.47 (1H, m), 2.43-2.12 (3H, m), 2.05-1.86 (2H, m), 1.86-1.60 (4H, m), 1.30 (3H, t, J=7 Hz).

(30e) Ethyl 8-trifluoromethanesulfonyloxy-1-oxaspiro[4.5]dec-7-ene-7-carboxylate

To a suspension of 72 mg of 55% sodium hydride (1.65 mmol)/3 ml of dichloromethane, was added a solution of 340 mg (1.50 mmol) of ethyl 8-oxo-1-oxaspiro[4.5]decane-7-carboxylate obtained in (29d) in 4 ml of dichloromethane with stirring under ice-cooling, followed by stirring for 1 hour at the same temperature. Subsequently, the reaction solution was cooled to −78° C., and 0.28 ml (1.65 mmol) of trifluoromethanesulfonic anhydride was added thereto. The mixture was stirred for 1 hour at the same temperature, and then warmed to room temperature. After ice water was added to the reaction solution to terminate the reaction, the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; ethyl acetate alone) to give 480 mg of the title compound as a pale yellow oil (yield: 89%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.26 (2H, q, J=7 Hz), 3.92-3.81 (2H, m), 2.74-2.63 (1H, m), 2.62-2.48 (2H, m), 2.45-2.34 (1H, m), 2.04-1.68 (6H, m), 1.32 (3H, t, J=7 Hz).

(30f) Ethyl 8-acetylthio-1-oxaspiro[4.5]dec-7-ene-7-carboxylate

Following the process described in Example (1a), ethyl 8-trifluoromethanesulfonyloxy-1-oxaspiro[4.5]dec-7-ene-7-carboxylate obtained in (30e) was used in place of ethyl 8-trifluoromethanesulfonyloxy-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate to give the title compound as a yellow oil (yield: 32%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.18 (2H, q, J=7 Hz), 3.91-3.83 (2H, m), 2.65-2.60 (1H, m), 2.60-2.51 (2H, m), 2.40-2.35 (1H, m), 2.32 (2.6H, s), 2.29 (0.4H, s), 2.00-1.93 (2H, m), 1.87-1.67 (4H, m), 1.28 (3H, t, J=7 Hz).

(30g) Ethyl 8-mercapto-1-oxaspiro[4.5]dec-7-ene-7-carboxylate

120 mg (0.42 mmol) of ethyl 8-acetylthio-1-oxaspiro[4.5] dec-7-ene-7-carboxylate obtained in (30f) was dissolved in 3 ml of ethanol, and 1 ml (4 mmol) of 4N hydrogen chloride/ dioxane solution was added thereto, followed by stirring for 4 hours at room temperature. The reaction solution was concentrated under reduced pressure and the residue was sub-

jected to silica gel column chromatography (solvent; hexane: ethyl acetate=3:1) to give 100 mg of the title compound as a pale yellow oil (98% yield).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.24-4.16 (2H, m), 4.12 (1H, s), 3.91-3.80 (2H, m), 2.84-2.71 (1H, m), 2.52-2.34 (3H, m), 2.01-1.90 (2H, m), 1.82-1.58 (4H, m), 1.23 (3H, t, J=7 Hz).

(30h) Ethyl 8-chlorosulfonyl-1-oxaspiro[4.5]dec-7-ene-7-carboxylate

100 mg (0.41 mmol) of ethyl 8-mercapto-1-oxaspiro[4.5] dec-7-ene-7-carboxylate obtained in (30f) was dissolved in 4 ml of solution mixture of acetic acid and water (acetic acid: water=1:1), and chlorine gas was blown into the reaction solution with stirring under ice-cooling for 15 minutes. Ice water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=3:1) to give 108 mg of the title compound as a colorless oil (yield: 85%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.28 (2H, q, J=7 Hz), 3.88 (2H, t, J=7 Hz), 2.92-2.81 (1H, m), 2.77-2.66 (1H, m), 1.58 (2H, m), 2.06-1.89 (3H, m), 1.80 (2H, t, 7 Hz), 1.77-1.67 (1H, m), 1.34 (3H, t, J=7 Hz).

(30i) Ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1-oxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity diastereomer), (high polarity diastereomer)

To a solution of 57 mg (0.39 mmol) of 2-chloro-4-fluoroaniline and 0.05 ml (0.39 mmol) of triethylamine in 1 ml of ethyl acetate, was added dropwise a solution of 108 mg (0.35 mmol) of ethyl 8-chlorosulfonyl-1-oxaspiro[4.5]dec-7-ene-7-carboxylate obtained in (29h) in 2 ml of ethyl acetate with stirring under ice-cooling, followed by stirring overnight at room temperature. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel thin layer chromatography (solvent; hexane:ethyl acetate=3:1) to give 12 mg of low polarity diastereomer of the title compound as a white powder and 20 mg of high polarity diastereomer of the title compound as an amorphous substance (yield: 8%, 14%).

(Low Polarity Diastereomer)

Melting point: 112-114° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.65 (1H, dd, J=9 Hz, 5 Hz), 7.14 (1H, dd, J=8 Hz, 3 Hz), 7.04-6.97 (1H, m), 6.95 (1H, s), 6.90 (1H, s), 4.45 (1H, dd, J=6 Hz, 2 Hz), 4.22-4.10 (2H, m), 3.96-3.88 (1H, m), 3.86-3.79 (1H, m), 2.41-2.33 (1H, m), 2.29-2.18 (1H, m), 2.13-2.01 (4H, m), 1.94-1.79 (2H, m), 1.25 (3H, t, J=7 Hz).

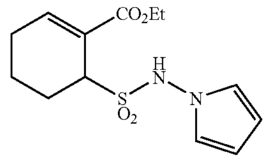
(High Polarity Diastereomer)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.66 (1H, dd, J=9 Hz, 5 Hz), 7.13 (1H, dd, J=8 Hz, 3 Hz), 7.04-6.96 (2H, m), 6.95 (1H, s), 4.36 (1H, d, J=5 Hz), 4.22-4.10 (2H, m), 4.03-3.96 (1H, m), 3.93-3.85 (1H, m), 2.56-2.48 (1H, m), 2.40-2.29 (1H, m), 2.06-1.63 (6H, m), 1.26 (3H, t, J=7 Hz).

Example 31

Ethyl 6-[N-(1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1057)



To a solution of 1.0 g (12.18 mmol) of 1H-pyrrol-1-ylamine and 1.8 ml (13.40 mmol) of triethylamine in 60 ml of ethyl acetate was added dropwise a solution of 3.6 g (12.18 mmol) of ethyl 2-chlorosulfonyl-1-cyclohexene-1-carboxylate (compound disclosed in the specification of Japanese Patent Application (Kokai) No. 2000-178246) in 12 ml of ethyl acetate with stirring under ice-cooling, followed by stirring overnight at room temperature. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=3:1) and the resulting solid was further washed with isopropyl ether to give 1.9 g of the title compound as a white powder (yield: 52%).

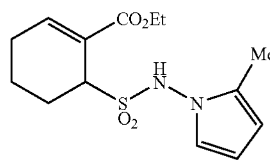
Melting point: 85-86° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

8.15 (1H, s), 7.44-7.42 (1H, m), 7.02 (2H, t, J=2 Hz), 6.17 (2H, t, J=2 Hz), 4.57-4.56 (1H, m), 4.29 (2H, q, J=7 Hz), 2.52-2.46 (2H, m), 2.32-2.23 (1H, m), 1.93-1.66 (3H, m), 1.34 (3H, t, J=7 Hz).

Example 32

Ethyl 6-[N-(2-methyl-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1176)



Following the process described in Example 31, 2-methyl-1H-pyrrol-1-ylamine was used in place of 1H-pyrrol-1-ylamine to give the title compound as a white powder (yield: 32%).

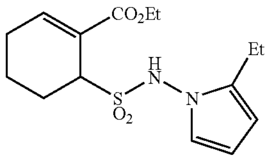
Melting point: 100-101° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.95 (1H, s), 7.43-7.39 (1H, m), 7.03-6.99 (1H, m), 6.07 (1H, t, J=4 Hz), 5.88-5.84 (1H, m), 4.60-4.55 (1H, m), 4.26 (2H, q, J=7 Hz), 2.56-2.43 (2H, m), 2.34-2.20 (1H, m), 2.29 (3H, s), 1.95-1.66 (3H, m), 1.33 (3H, t, J=7 Hz).

Example 33

Ethyl 6-[N-(2-ethyl-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1193)



Following the process described in Example 31, 2-ethyl-1H-pyrrol-1-ylamine was used in place of 1H-pyrrol-1-ylamine to give the title compound as a white powder (yield: 51%).

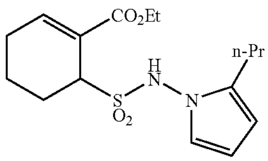
Melting point: 77-78° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.97 (1H, s), 7.46-7.41 (1H, m), 7.04-7.01 (1H, m), 6.13 (1H, t, J=4 Hz), 5.92-5.87 (1H, m), 4.62-4.57 (1H, m), 4.28 (2H, q, J=7 Hz), 2.79-2.64 (2H, m), 2.58-2.42 (2H, m), 2.35-2.21 (1H, m), 1.95-1.65 (3H, m), 1.33 (3H, t, J=7 Hz), 1.24 (3H, t, J=8 Hz).

Example 34

Ethyl 6-[N-(2-propyl-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1210)



Following the process described in Example 31, 2-propyl-1H-pyrrol-1-ylamine was used in place of 1H-pyrrol-1-ylamine to give the title compound as a white powder (yield: 31%).

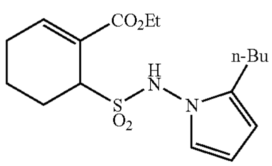
Melting point: 66-68° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.97 (1H, s), 7.46-7.41 (1H, m), 7.04-7.01 (1H, m), 6.12 (1H, t, J=3 Hz), 5.92-5.87 (1H, m), 4.62-4.57 (1H, m), 4.27 (2H, q, J=7 Hz), 2.73-2.62 (2H, m), 2.57-2.43 (2H, m), 2.34-2.21 (1H, m) 1.95-1.63 (5H, m), 1.33 (3H, t, J=7 Hz), 0.99 (3H, t, J=7 Hz).

Example 35

Ethyl 6-[N-(2-butyl-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1227)



Following the process described in Example 31, 2-butyl-1H-pyrrol-1-ylamine was used in place of 1H-pyrrol-1-ylamine to give the title compound as a white powder (yield: 26%).

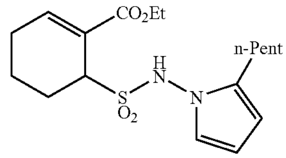
Melting point: 49-50° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.94 (1H, s), 7.43-7.39 (1H, m), 7.01-6.98 (1H, m), 6.11-6.08 (1H, m), 5.89-5.85 (1H, m), 4.60-4.55 (1H, m), 4.26 (2H, q, J=7 Hz), 2.71-2.65 (2H, m), 2.56-2.43 (2H, m), 2.33-2.20 (1H, m) 1.94-1.57 (5H, m), 1.45-1.35 (2H, m), 1.32 (3H, t, J=7 Hz), 0.93 (3H, t, J=7 Hz).

Example 36

Ethyl 6-[N-(2-pentyl-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1244)



Following the process described in Example 31, 2-pentyl-1H-pyrrol-1-ylamine obtained in Reference Example 6 was used in place of 1H-pyrrol-1-ylamine to give the title compound as a white powder (yield: 33%).

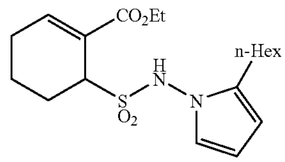
Melting point: 60-61° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.96 (1H, s), 7.46-7.41 (1H, m), 7.04-7.00 (1H, m), 6.12 (1H, t, J=3 Hz), 5.92-5.86 (1H, m), 4.62-4.56 (1H, m), 4.28 (2H, q, J=7 Hz), 2.72-2.65 (2H, m), 2.57-2.44 (2H, m), 2.34-2.21 (1H, m), 1.95-1.59 (5H, m), 1.42-1.29 (4H, m), 1.34 (3H, t, J=7 Hz), 0.89 (3H, t, J=7 Hz).

Example 37

Ethyl 6-[N-(2-hexyl-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1261)



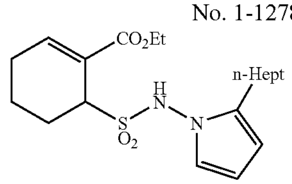
Following the process described in Example 31, 2-hexyl-1H-pyrrol-1-ylamine obtained in Reference Example 7 was used in place of 1H-pyrrol-1-ylamine to give the title compound as a yellow oil (yield: 46%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.93 (1H, s), 7.43-7.39 (1H, m), 7.01-6.98 (1H, m), 6.12-6.08 (1H, m), 5.89-5.85 (1H, m), 4.60-4.55 (1H, m), 4.27 (2H, q, J=' Hz), 2.71-2.64 (2H, m), 2.56-2.43 (2H, m), 2.33-2.21 (1H, m), 1.91-1.58 (5H, m), 1.42-1.27 (6H, m), 1.33 (3H, t, J=7 Hz), 0.88 (3H, t, J=7 Hz).

Example 38

Ethyl 6-[N-(2-heptyl-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1278)



Following the process described in Example 31, 2-heptyl-1H-pyrrol-1-ylamine obtained in Reference Example 8 was

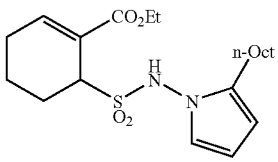
used in place of 1H-pyrrol-1-ylamine to give the title compound as a colorless oil (yield: 13%).

[1]H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.97 (1H, s), 7.46-7.41 (1H, m), 7.04-7.01 (1H, m), 6.11 (1H, t, J=3 Hz), 5.96-5.86 (1H, m), 4.62-4.56 (1H, m), 4.28 (2H, q, J=7 Hz), 2.72-2.62 (2H, m), 2.58-2.43 (2H, m), 2.35-2.21 (1H, m), 1.94-1.59 (5H, m), 1.41-1.22 (8H, m), 1.33 (3H, t, J=7 Hz), 0.88 (3H, t, J=7 Hz).

Example 39

Ethyl 6-[N-(2-octyl-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1295)



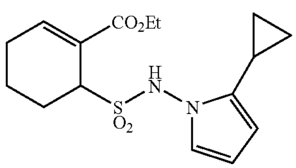
Following the process described in Example 31, 2-octyl-1H-pyrrol-1-ylamine obtained in Reference Example 8 was used in place of 1H-pyrrol-1-ylamine to give the title compound as a pale yellow oil (yield: 18%).

[1]H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.96 (1H, s), 7.46-7.41 (1H, m), 7.04-7.00 (1H, m), 6.11 (1H, t, J=4 Hz), 5.91-5.86 (1H, m), 4.61-4.57 (1H, m), 4.28 (2H, q, J=7 Hz), 2.71-2.64 (2H, m), 2.57-2.44 (2H, m), 2.34-2.20 (1H, m), 1.95-1.58 (5H, m), 1.42-1.19 (10H, m), 1.33 (3H, t, J=7 Hz), 0.88 (3H, t, J=7 Hz).

Example 40

Ethyl 6-[N-(2-cyclopropyl-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1312)



Following the process described in Example 31, 2-cyclopropyl-1H-pyrrol-1-ylamine obtained in Reference Example 10 was used in place of 1H-pyrrol-1-ylamine to give the title compound as a pale pink powder (yield: 42%).

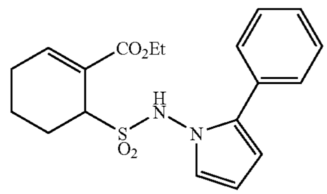
Melting point: 95-96° C.

[1]H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.87 (1H, s), 7.41-7.37 (1H, m), 6.98-6.95 (1H, m), 6.05-6.02 (1H, m), 5.69-5.66 (1H, m), 4.66-4.61 (1H, m), 4.25 (2H, q, J=7 Hz), 2.60-2.43 (2H, m), 2.34-2.20 (1H, m), 2.05-1.87 (2H, m), 1.82-1.68 (2H, m), 1.31 (3H, t, J=7 Hz), 0.94-0.82 (2H, m), 0.73-0.65 (1H, m), 0.59-0.51 (1H, m).

Example 41

Ethyl 6-[N-(2-phenyl-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1329)



Following the process described in Example 31, 2-phenyl-1H-pyrrol-1-ylamine was used in place of 1H-pyrrol-1-ylamine to give the title compound as a pale yellow powder (yield: 21%).

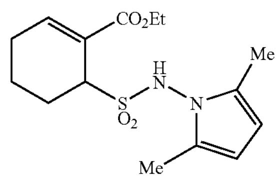
Melting point: 160-161° C.

[1]H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.99 (1H, s), 7.57 (2H, d, J=8 Hz), 7.39 (2H, t, J=8 Hz), 7.33-7.27 (2H, m), 7.14-7.11 (1H, m), 6.32-6.28 (1H, m), 6.25 (1H, t, J=4 Hz), 4.22 (2H, q, J=7 Hz), 4.18-4.14 (1H, m), 2.44-2.32 (1H, m), 2.24-2.07 (2H, m), 1.91-1.75 (1H, m), 1.67-1.51 (1H, m), 1.40-1.29 (1H, m), 1.28 (3H, t, J=7 Hz).

Example 42

Ethyl 6-[N-(2,5-dimethyl-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1346)



Following the process described in Example 31, 2,5-dimethyl-1H-pyrrol-1-ylamine was used in place of 1H-pyrrol-1-ylamine to give the title compound as a white powder (yield: 29%).

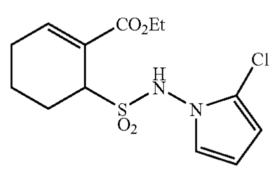
Melting point: 96-97° C.

[1]H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.88 (1H, s), 7.40-7.35 (1H, m), 5.75 (2H, s), 4.58-4.52 (1H, m), 4.24 (2H, q, 7 Hz), 2.69-2.61 (1H, m), 2.53-2.42 (1H, m), 2.33-2.19 (1H, m), 2.26 (6H, s), 2.02-1.91 (1H, m), 1.86-1.73 (2H, m), 1.30 (3H, t, J=7 Hz).

Example 43

Ethyl 6-[N-(2-chloro-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1091)



150 mg (0.503 mmol) of ethyl 6-[N-(1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate obtained in Example

31 was dissolved in 3 ml of tetrahydrofuran, and 70 mg (0.528 mmol) of N-chlorosuccinimide was added thereto with stirring under ice-cooling, followed by stirring overnight at room temperature. Water was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel thin layer chromatography (solvent; hexane:ethyl acetate=2:1) and the resulting solid was further washed with isopropyl ether to give 50 mg of the title compound as a white powder (yield: 30%).

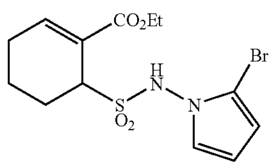
Melting point: 60-61° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.91 (1H, s), 7.43-7.37 (1H, m), 7.04 (1H, dd, J=4 Hz, 2 Hz), 6.14 (1H, t, J=4 Hz), 6.10 (1H, dd, J=4 Hz, 2 Hz), 4.65-4.61 (1H, m), 4.26 (2H, q, J=7 Hz), 2.61-2.44 (2H, m), 2.33-2.21 (1H, m), 2.05-1.90 (1H, m), 1.83-1.71 (2H, m), 1.30 (3H, t, J=7 Hz).

Example 44

Ethyl 6-[N-(2-bromo-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (exemplified compound No. 1-1108)



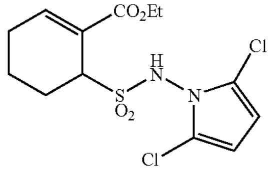
Following the process described in Example 43, N-bromosuccinimide was used in place of N-chlorosuccinimide to give the title compound as a white powder (yield: 50%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.85 (1H, s), 7.42-7.38 (1H, m), 7.15 (1H, dd, J=4 Hz, 2 Hz), 6.22-6.17 (2H, m), 4.67-4.62 (1H, m), 4.25 (2H, q, J=7 Hz), 2.60-2.44 (2H, m), 2.33-2.20 (1H, m), 2.05-1.92 (1H, m), 1.83-1.70 (2H, m), 1.30 (3H, t, J=7 Hz).

Example 45

Ethyl 6-[N-(2,5-dichloro-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1142)



Following the process described in Example 42, 2.1 equivalent of N-chlorosuccinimide was used relative to ethyl 6-[N-(1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate obtained in Example 31 to give the title compound as a pale yellow oil (yield: 25%).

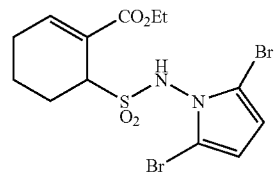
Melting point: 144-145° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

8.08 (1H, s), 7.39-7.33 (1H, m), 6.07 (2H, s), 4.89-4.83 (1H, m), 4.24 (2H, q, J=7 Hz), 2.67-2.58 (1H, m), 2.52-2.42 (1H, m), 2.31-2.19 (1H, m), 2.03-1.88 (1H, m), 1.87-1.72 (2H, m), 1.29 (3H, t, J=7 Hz).

Example 46

Ethyl 6-[N-(2,5-dibromo-1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate (Exemplified compound No. 1-1159)



Following the process described in Example 44, 2.1 equivalent of N-bromosuccinimide was used relative to ethyl 6-[N-(1H-pyrrol-1-yl)sulfamoyl]-1-cyclohexene-1-carboxylate obtained in Example 31 to give the title compound as a white powder (yield: 3%).

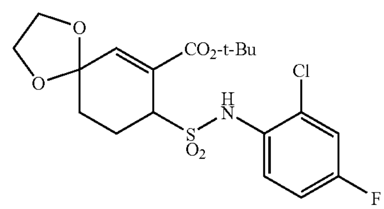
Melting point: 123-124° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

8.05 (1H, s), 7.40-7.35 (1H, m), 6.24 (2H, s), 5.02-4.95 (1H, m), 4.25 (2H, q, J=7 Hz), 2.69-2.60 (1H, m), 2.53-2.42 (1H, m), 2.33-2.19 (1H, m), 2.02-1.90 (1H, m), 1.87-1.72 (2H, m), 1.29 (3H, t, J=7 Hz).

Example 47

t-Butyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 3-89)



(47a) 8-[N-(2-Chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylic acid

1.8 g (4.29 mmol) of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 1 was dissolved in 60 ml of a water-tetrahydrofuran (1:1) solution, and 900 mg (21.45 mmol) of lithium hydroxide was added thereto, followed by stirring for 7 hours at 50° C. The reaction solution was cooled with ice, it was then made acidic by addition of 1N hydrochloric acid, and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was washed with hexane to give 1.43 g of the title compound as a pale brown powder (yield: 85%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.68 (1H, dd, J=9 Hz, 5 Hz), 7.16 (1H, dd, J=8 Hz, 3 Hz), 7.04-6.93 (3H, m), 4.36 (1H, d, J=5 Hz), 4.16-4.02 (3H, m), 3.97-3.88 (1H, m), 2.57-2.45 (3H, m), 2.25-2.13 (1H, m), 1.90-1.82 (1H, m).

(47b) t-Butyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate

100 mg (0.26 mmol) of 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylic acid obtained in (47a) was dissolved in 2 ml of toluene, and 1 ml of N,N-dimethylformamide di-t-butyl acetal was added thereto, followed by stirring for 3 hours at 100° C. After the reaction solution was cooled to room temperature, water was added and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel thin layer chromatography (solvent; dichloromethane:methanol=1:50) to give 52 mg of the title compound as a white amorphous substance (yield: 45%).

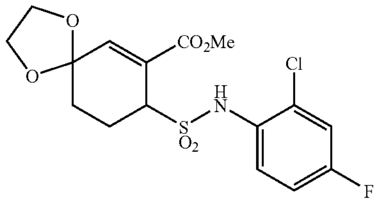
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.64 (1H, dd, J=9 Hz, 5 Hz), 7.15 (1H, dd, J=8 Hz, 3 Hz), 7.05-6.98 (2H, m), 6.71 (1H, s), 4.42-4.38 (1H, m), 4.13-4.01 (3H, m), 3.95-3.88 (1H, m), 2.51-2.40 (2H, m), 2.21-2.10 (1H, m), 1.86-1.79 (1H, m), 1.46 (9H, s).

Following the process described in Example (47b), various corresponding acetals were used in place of N,N-dimethylformamide di-t-butyl acetal to synthesize the compounds of Examples 48 to 51.

Example 48

Methyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 3-73)



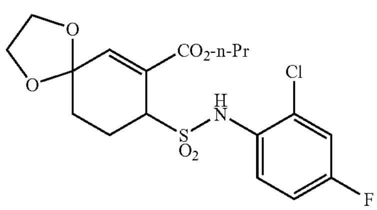
White powder (yield: 50%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.67 (1H, dd, J=9 Hz, 5 Hz), 7.16 (1H, dd, J=8 Hz, 3 Hz), 7.06-6.99 (1H, m), 6.98 (1H, s), 6.84 (1H, s), 4.43-4.38 (1H, m), 4.15-3.99 (3H, m), 3.95-3.88 (1H, m), 3.73 (3H, s), 2.56-2.43 (2H, m), 2.24-2.12 (1H, m), 1.88-1.79 (1H, m).

Example 49

Propyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 3-77)



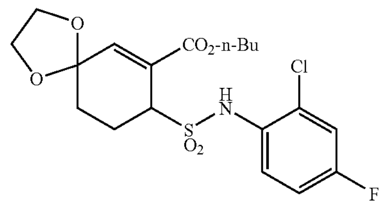
White amorphous substance (yield: 18%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.67 (1H, dd, J=9 Hz, 5 Hz), 7.16 (1H, dd, J=8 Hz, 3 Hz), 7.05-6.97 (2H, m), 6.81 (1H, s), 4.42 (1H, d, J=5 Hz), 4.16-3.99 (5H, m), 3.95-3.88 (1H, m), 2.55-2.44 (2H, m), 2.24-2.11 (1H, m), 1.88-1.81 (1H, m), 1.71-1.60 (2H, m), 0.94 (3H, t, J=7 Hz).

Example 50

Butyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 3-81)



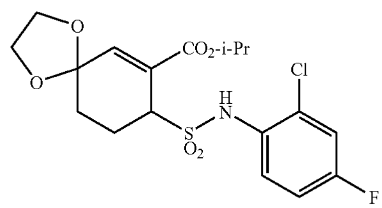
White powder (yield: 26%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.66 (1H, dd, J=9 Hz, 5 Hz), 7.16 (1H, dd, J=8 Hz, 3 Hz), 7.05-6.96 (2H, m), 6.80 (1H, s), 4.42 (1H, d, J=5 Hz), 4.20-4.00 (5H, m), 3.95-3.87 (1H, m), 2.55-2.44 (2H, m), 2.24-2.11 (1H, m), 1.88-1.80 (1H, m), 1.66-1.57 (2H, m), 1.43-1.32 (2H, m), 0.93 (3H, t, J=7 Hz).

Example 51

Isopropyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 3-85)



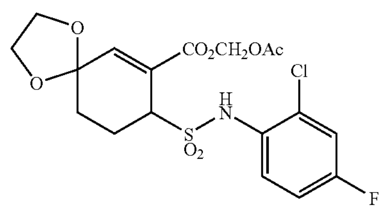
White powder (yield: 21%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.66 (1H, dd, J=9 Hz, 5 Hz), 7.16 (1H, dd, J=8 Hz, 3 Hz), 7.06-6.98 (2H, m), 6.78 (1H, s), 5.11-4.99 (1H, m), 4.42 (1H, d, J=5 Hz), 4.15-3.99 (3H, m), 3.95-3.88 (1H, m), 2.55-2.43 (2H, m), 2.24-2.11 (1H, m), 1.99-1.79 (1H, m), 1.26 (3H, d, J=2 Hz), 1.24 (3H, d, J=2 Hz).

Example 52

Acetoxymethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 3-93)



1 g (2.55 mmol) of 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylic acid

obtained in Example 47a was dissolved in 20 ml of acetonitrile, and 0.50 ml (5.10 mmol) of bromomethyl acetate, 499 mg (1.53 mmol) of cesium carbonate and 471 mg (1.28 mmol) of tetrabutylammonium iodide were added thereto, followed by stirring for 1 hour at room temperature. 0.1 N hydrochloric acid was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; dichloromethane:methanol=49:1) to give 833 mg of the title compound as an amorphous substance (yield: 70%).

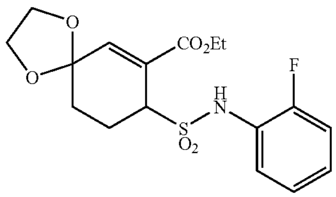
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.67 (1H, dd, J=9 Hz, 5 Hz), 7.18 (1H, dd, J=8 Hz, 3 Hz), 7.08-7.02 (1H, m), 7.01 (1H, s), 6.92 (1H, s), 5.80 (2H, s), 4.41 (1H, dd, J=6 Hz, 2 Hz), 4.15-4.01 (3H, m), 3.94-3.88 (1H, m), 2.48 (1H, td, J=14 Hz, 4 Hz), 2.44-2.37 (1H, m), 2.22-2.14 (1H, m), 2.12 (3H, s), 1.85-1.79 (1H, m).

Following the process described in Example (1d), various corresponding anilines were used in place of 2-chloro-4-fluoroaniline to synthesize the compounds of Examples 53 to 121.

Example 53

Ethyl 8-[N-(2-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2217)



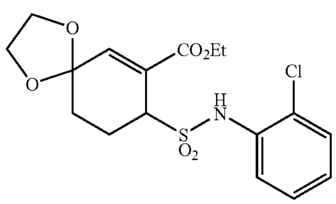
Oil (yield: 61%)

^{1}H-NMR spectrum (400 MHz, CDC_3) δ ppm:

7.67-7.62 (1H, m), 7.17-7.09 (3H, m), 6.96 (1H, d, J=3 Hz), 6.83 (1H, t, J=1 Hz), 4.43-4.40 (1H, m), 4.24-4.01 (5H, m), 3.95-3.89 (1H, m), 2.55-2.41 (2H, m), 2.21-2.10 (1H, m), 1.89-1.81 (1H, m), 1.27 (3H, t, J=7 Hz).

Example 54

Ethyl 8-[N-(2-chlorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-188)



Pale brown powder (yield: 69%)

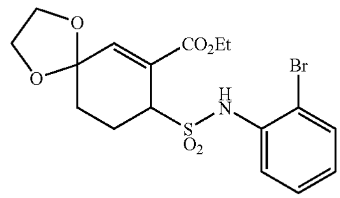
Melting point: 157-160° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.70 (1H, dd, J=8 Hz, 1 Hz), 7.39 (1H, dd, J=8 Hz, 2 Hz), 7.31-7.26 (1H, m), 7.10-7.05 (2H, m), 6.83 (1H, t, J=1 Hz), 4.49-4.46 (1H, m), 4.24-4.02 (5H, m), 3.95-3.89 (1H, m), 2.60-2.48 (2H, m), 2.24-2.13 (1H, m), 1.88-1.81 (1H, m), 1.24 (3H, t, J=7 Hz).

Example 55

Ethyl 8-[N-(2-bromophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1374)



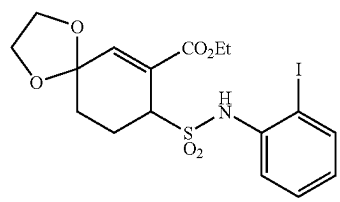
Oil (yield: 59%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.70 (1H, dd, J=8 Hz, 1 Hz), 7.55 (1H, dd, J=8 Hz, 2 Hz), 7.36-7.30 (1H, m), 7.04-6.98 (2H, m), 6.83 (1H, t, J=1 Hz), 4.50-4.47 (1H, m), 4.23-4.01 (5H, m), 3.95-3.88 (1H, m), 2.62-2.49 (2H, m), 2.24-2.13 (1H, m), 1.88-1.81 (1H, m), 1.24 (3H, t, J=7 Hz).

Example 56

Ethyl 8-[N-(2-iodophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2224)



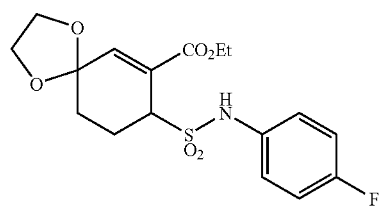
Amorphous substance (yield: 53%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.79 (1H, dd, J=8 Hz, 1 Hz), 7.67 (1H, dd, J=8 Hz, 1 Hz), 7.38-7.33 (1H, m), 6.88-6.82 (3H, m), 4.49 (1H, d, J=5 Hz), 4.24-4.01 (5H, m), 3.95-3.88 (1H, m), 2.63-2.49 (2H, m), 2.24-2.13 (1H, m), 1.88-1.81 (1H, m), 1.24 (3H, t, J=7 Hz).

Example 57

Ethyl 8-[N-(4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-100)



White powder (yield: 87%)

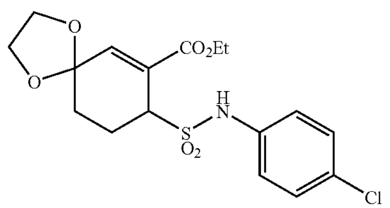
Melting point: 141-146° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.38-7.33 (2H, m), 7.07-7.01 (3H, m), 6.87 (1H, t, J=1 Hz), 4.30-4.21 (3H, m), 4.14-4.01 (3H, m), 3.95-3.89 (1H, m), 2.45-2.38 (1H, m), 2.27 (1H, td, J=14 Hz, 3 Hz), 2.09-1.99 (1H, m), 1.87-1.80 (1H, m), 1.33 (3H, t, J=7 Hz).

Example 58

Ethyl 8-[N-(4-chlorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2231)



White powder (yield: 81%)

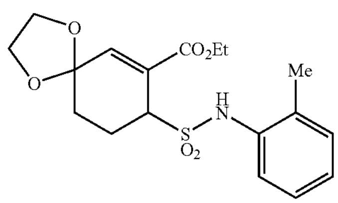
Melting point: 153-156° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.31 (4H, s), 7.03 (1H, s), 6.87 (1H, t, J=1 Hz), 4.29-4.19 (3H, m), 4.14-4.02 (3H, m), 3.95-3.89 (1H, m), 2.47-2.40 (1H, m), 2.27 (1H, td, J=14 Hz, 3 Hz), 2.10-2.00 (1H, m), 1.88-1.81 (1H, m), 1.32 (3H, t, J=7 Hz).

Example 59

Ethyl 8-[N-(2-methylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2238)



White powder (yield: 75%)

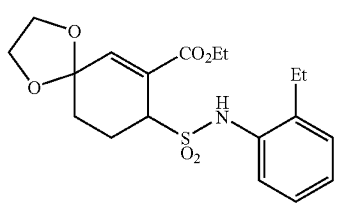
Melting point: 101-104° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.56-7.53 (1H, m), 7.23-7.18 (2H, m), 7.11-7.06 (1H, m), 6.85 (1H, t, J=1 Hz), 6.62 (1H, s), 4.44 (1H, dd, J=6 Hz, 2 Hz), 4.25-4.01 (5H, m), 3.95-3.89 (1H, m), 2.55-2.48 (1H, m), 2.42 (1H, td, J=14 Hz, 4 Hz), 2.34 (3H, s), 2.19-2.09 (1H, m), 1.88-1.81 (1H, m), 1.26 (3H, t, J=7 Hz).

Example 60

Ethyl 8-[N-(2-ethylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2245)



White powder (yield: 66%)

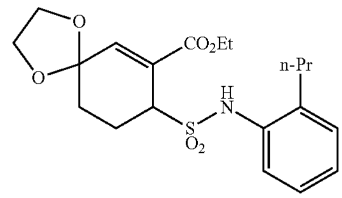
Melting point: 83-87° C.

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.54 (1H, dd, J=8 Hz, 1 Hz), 7.25-7.19 (2H, m), 7.14 (1H, td, J=7 Hz, 1 Hz), 6.85 (1H, s), 6.63 (1H, s), 4.47 (1H, dd, J=6 Hz, 2 Hz), 4.25-4.02 (5H, m), 2.75-2.66 (2H, m), 2.54-2.48 (1H, m), 2.43 (1H, td, J=14 Hz, 4 Hz), 2.19-2.11 (1H, m), 1.87-1.81 (1H, m), 1.28-1.23 (6H, m).

Example 61

Ethyl 8-[N-(2-propylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1989)



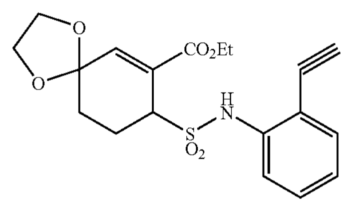
Oil (53% yield)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.55-7.52 (1H, m), 7.23-7.18 (2H, m), 7.14-7.09 (1H, m), 6.85 (1H, t, J=1 Hz), 6.64 (1H, s), 4.48-4.44 (1H, m), 4.24-4.02 (5H, m), 3.95-3.89 (1H, m), 2.67-2.62 (2H, m), 2.54-2.39 (2H, m), 2.20-2.10 (1H, m), 1.87-1.81 (1H, m), 1.69-1.58 (2H, m), 1.26 (3H, t, J=7 Hz), 0.99 (3H, t, J=7 Hz).

Example 62

Ethyl 8-[N-(2-ethynylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2252)



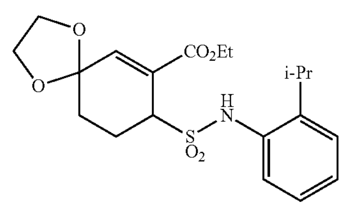
Oil (yield: 19%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.66 (1H, dd, J=8 Hz, 1 Hz), 7.47 (1H, dd, J=8 Hz, 2 Hz), 7.37 (1H, td, J=8 Hz, 2 Hz), 7.21 (1H, s), 7.07 (1H, td, J=8 Hz, 1 Hz), 6.82 (1H, t, J=1 Hz), 4.52-4.49 (1H, m), 4.22-4.01 (5H, m), 3.95-3.88 (1H, m), 3.49 (1H, s), 2.65-2.50 (2H, m), 2.24-2.13 (1H, m), 1.88-1.81 (1H, m), 1.22 (3H, t, J=7 Hz).

Example 63

Ethyl 8-[N-(2-isopropylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2259)



Pale brown powder (yield: 65%)

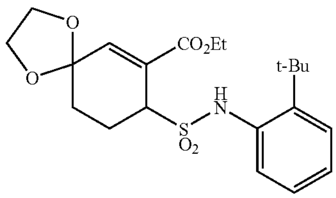
Melting point: 115-118° C.

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.53-7.49 (1H, m), 7.34-7.30 (1H, m), 7.23-7.17 (2H, m), 6.86 (1H, s), 6.69 (1H, s), 4.47 (1H, dd, J=6 Hz, 2 Hz), 4.27-4.02 (5H, m), 3.95-3.89 (1H, m), 3.33-3.24 (1H, m), 2.53-2.47 (1H, m), 2.42 (1H, td, J=14 Hz, 3 Hz), 2.18-2.10 (1H, m), 1.86-1.81 (1H, m), 1.29-1.21 (9H, m).

Example 64

Ethyl 8-[N-(2-t-butylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2266)



White powder (yield: 53%)

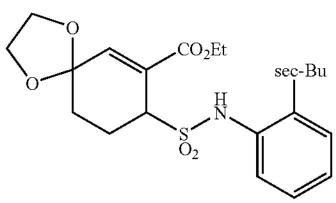
Melting point: 117-120° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.45 (1H, dd, J=8 Hz, 1 Hz), 7.38 (1H, dd, J=8 Hz, 2 Hz), 7.23 (1H, td, J=8 Hz, 2 Hz), 7.12-7.07 (1H, m), 6.86 (1H, t, J=1 Hz), 6.64 (1H, s), 4.64-4.61 (1H, m), 4.24-4.03 (5H, m), 3.97-3.90 (1H, m), 2.65-2.53 (2H, m), 2.28-2.18 (1H, m), 1.90-1.83 (1H, m), 1.45 (9H, s), 1.23 (3H, t, J=7 Hz).

Example 65

Ethyl 8-[N-(2-sec-butylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2273)



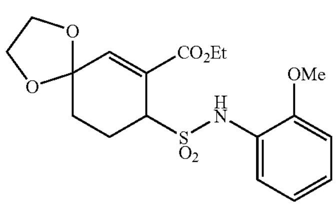
Oil (71% yield)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.54-7.49 (1H, m), 7.29-7.16 (3H, m), 6.86 (1H, dt, J=5 Hz, 1 Hz), 6.68 (1H, d, J=10 Hz), 4.47-4.44 (1H, m), 4.27-4.02 (5H, m) 3.95-3.89 (1H, m), 3.12-2.95 (1H, m), 2.53-2.35 (2H, m), 2.19-2.07 (1H, m), 1.86-1.80 (1H, m), 1.70-1.55 (2H, m), 1.31-1.19 (6H, m), 0.91-0.80 (3H, m).

Example 66

Ethyl 8-[N-(2-methoxyphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2280)



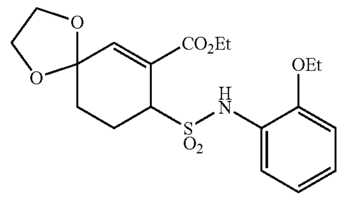
White powder (yield: 70%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.57 (1H, dd, J=8 Hz, 2 Hz), 7.11-7.05 (2H, m), 6.96 (1H, td, J=8 Hz, 1 Hz), 6.89 (1H, dd, J=8 Hz, 1 Hz), 6.79 (1H, t, J=1 Hz), 4.44 (1H, d, J=4 Hz), 4.21-4.00 (5H, m), 3.94-3.84 (4H, m), 2.58 (1H, td, J=14 Hz, 4 Hz), 2.50-2.43 (1H, m), 2.18-2.08 (1H, m), 1.84-1.77 (1H, m), 1.23 (3H, t, J=7 Hz).

Example 67

Ethyl 8-[N-(2-ethoxyphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2287)



White powder (yield: 60%)

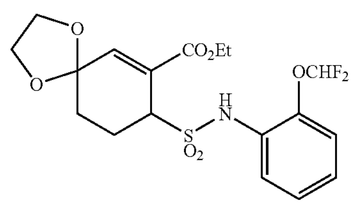
Melting point: 129-134° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.58 (1H, dd, J=8 Hz, 2 Hz), 7.12 (1H, s), 7.06 (1H, td, J=8 Hz, 2 Hz), 6.95 (1H, td, J=8 Hz, 2 Hz), 6.87 (1H, dd, J=8 Hz, 1 Hz), 6.79 (1H, t, J=1 Hz), 4.45-4.42 (1H, m), 4.20-4.00 (7H, m), 3.94-3.87 (1H, m), 2.57 (1H, td, J=14 Hz, 4 Hz), 2.50-2.44 (1H, m), 2.18-2.08 (1H, m), 1.85-1.78 (1H, m), 1.45 (3H, t, J=7 Hz), 1.23 (3H, t, J=7 Hz)

Example 68

Ethyl 8-[N-(2-difluoromethoxyphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2294)



White powder (yield: 48%)

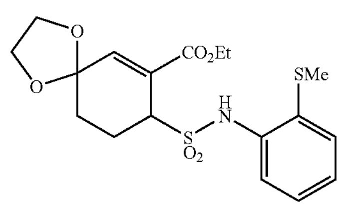
Melting point: 85-88° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.69 (1H, dd, J=8 Hz, 2 Hz), 7.25-7.08 (4H, m), 6.84 (1H, s), 6.57 (1H, dd, J=74 Hz, 73 Hz), 4.44-4.41 (1H, m), 4.21-4.02 (5H, m), 3.95-3.89 (1H, m), 2.57-2.44 (2H, m), 2.21-2.10 (1H, m), 1.90-1.82 (1H, m), 1.26 (3H, t, J=7 Hz).

Example 69

Ethyl 8-[N-(2-methylsulfanylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2301)



White powder (yield: 56%)

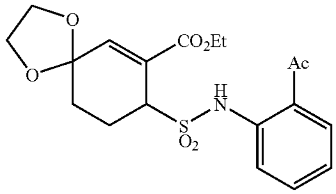
Melting point: 93-95° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.70 (1H, s), 7.63 (1H, dd, J=8 Hz, 1 Hz), 7.51 (1H, dd, J=8 Hz, 2 Hz), 7.33-7.28 (1H, m), 7.08 (1H, td, J=8 Hz, 1 Hz), 6.82 (1H, q, J=1 Hz), 4.50 (1H, d, J=4 Hz), 4.21-4.01 (5H, m), 3.95-3.88 (1H, m), 2.65-2.50 (2H, m), 2.38 (3H, s), 2.23-2.12 (1H, m), 1.88-1.81 (1H, m), 1.25-1.21 (3H, m).

Example 70

Ethyl 8-[N-(2-acetylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2308)



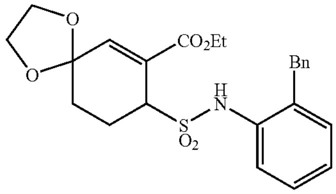
Oil (yield: 25%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

11.46 (1H, s), 7.91 (1H, dd, J=8 Hz, 1 Hz), 7.85 (1H, dd, J=8 Hz, 1 Hz), 7.59-7.54 (1H, m), 7.15-7.10 (1H, m), 6.80 (1H, t, J=1 Hz), 4.50-4.47 (1H, m), 4.16-4.00 (5H, m), 3.94-3.88 (1H, m), 2.68-2.59 (4H, m), 2.56-2.49 (1H, m), 2.20-2.09 (1H, m), 1.87-1.80 (1H, m), 1.25 (3H, t, J=7 Hz).

Example 71

Ethyl 8-[N-(2-benzylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2315)



White powder (yield: 73%)

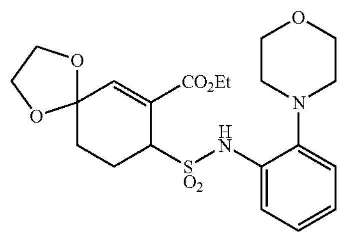
Melting point: 127-129° C.

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.58 (1H, dd, J=8 Hz, 1 Hz), 7.32-7.13 (8H, m), 6.80 (1H, s), 6.50 (1H, s), 4.36 (1H, dd, J=6 Hz, 2 Hz), 4.23-4.00 (7H, m), 3.93-3.87 (1H, m), 2.36 (1H, td, J=14 Hz, 4 Hz), 2.19-2.13 (1H, m), 2.03-1.94 (1H, m), 1.76-1.70 (1H, m), 1.26 (3H, t, J=7 Hz).

Example 72

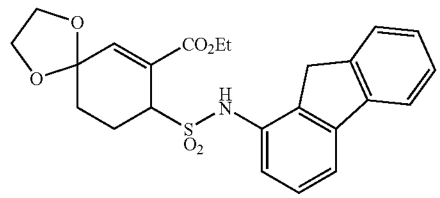
Ethyl 8-{N-[2-(morpholin-4-yl)phenyl]sulfamoyl}-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2322)



White powder (yield: 71%)
Melting point: 118-121° C.
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:
8.10 (1H, s), 7.58 (1H, dd, J=8 Hz, 2 Hz), 7.23 (1H, dd, J=8 Hz, 2 Hz), 7.20-7.15 (1H, m), 7.07 (1H, td, J=8 Hz, 2 Hz), 6.82 (1H, t, 1 Hz), 4.47-4.44 (1H, m), 4.15-4.00 (5H, m), 3.95-3.85 (5H, m), 2.92-2.83 (4H, m), 2.59-2.50 (2H, m), 2.24-2.12 (1H, m), 1.90-1.82 (1H, m), 1.23 (3H, t, J=7 Hz).

Example 73

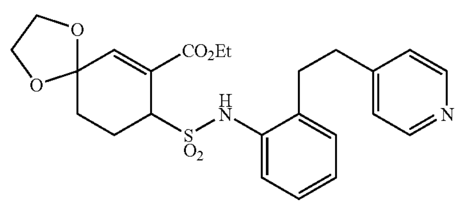
Ethyl 8-[N-(9H-fluoren-1-yl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2329)



Pale brown powder (yield: 60%)
Melting point: 156-160° C.
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:
7.78 (1H, d, J=7 Hz), 7.62 (1H, d, J=8 Hz), 7.58 (1H, d, J=7 Hz), 7.54 (1H, d, J=8 Hz), 7.42-7.37 (2H, m), 7.34 (1H, td, J=7 Hz, 1 Hz), 6.92 (1H, s), 6.86 (1H, s), 4.45 (1H, dd, J=6 Hz, 2 Hz), 4.22-4.00 (5H, m), 3.96 (2H, s), 3.94-3.89 (1H, m), 2.56-2.50 (1H, m), 2.37 (1H, td, J=14 Hz, 3 Hz), 2.17-2.08 (1H, m), 1.88-1.82 (1H, m), 1.26 (3H, t, J=7 Hz).

Example 74

Ethyl 8-(N-{2-[2-(pyridin-4-yl)ethyl]phenyl}sulfamoyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2336)

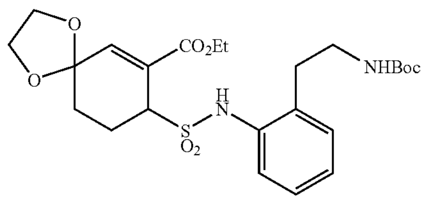


White powder (yield: 26%)
Melting point: 77-80° C.
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

8.50-8.47 (2H, m), 7.54-7.52 (1H, m), 7.26-7.22 (1H, m), 7.19-7.13 (4H, m), 6.89 (1H, t, J=1 Hz), 6.80 (1H, s), 4.43 (1H, dd, J=6 Hz, 3 Hz), 4.25-4.18 (2H, m), 4.14-4.03 (3H, m), 3.96-3.90 (1H, m), 3.15-3.00 (2H, m), 2.99-2.89 (2H, m), 2.54-2.48 (1H, m), 2.33 (1H, td, J=14 Hz, 3 Hz), 2.17-2.09 (1H, m), 1.88-1.82 (1H, m), 1.29 (3H, t, J=7 Hz).

Example 75

Ethyl 8-(N-{2-[2-(t-butoxycarbonylamino) ethyl] phenyl}sulfamoyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2343)



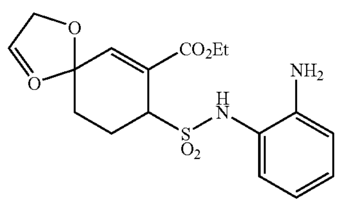
Amorphous substance (yield: 65%)

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

8.00 (1H, s), 7.62 (1H, d, J=8 Hz), 7.24 (1H, td, J=8 Hz, 2 Hz), 7.17 (1H, d, J=7 Hz), 7.10 (1H, t, J=7 Hz), 6.83 (1H, s), 4.90 (1H, brs), 4.46 (1H, d, J=5 Hz), 4.23-4.01 (5H, m), 3.94-3.88 (1H, m), 3.27 (2H, q, J=7 Hz), 2.96-2.83 (2H, m), 2.59-2.52 (2H, m), 2.18-2.09 (1H, m), 1.83-1.78 (1H, m), 1.48-1.41 (9H, m), 1.27 (3H, t, J=7 Hz).

Example 76

Ethyl 8-[N-(2-aminophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2350)



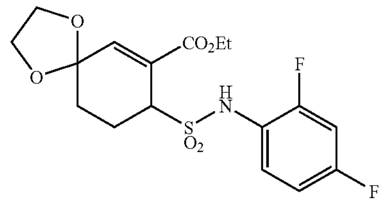
Oil (yield: 13%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.39 (1H, dd, J=8 Hz, 2 Hz), 7.11-7.06 (1H, m), 6.89 (1H, t, J=1 Hz), 6.79-6.73 (2H, m), 4.46 (1H, dd, J=6 Hz, 3 Hz), 4.31-3.86 (3H, m), 4.28 (2H, q, J=7 Hz), 4.11-4.02 (3H, m), 3.95-3.89 (1H, m), 2.48-2.41 (1H, m), 2.24 (1H, td, J=14 Hz, 3 Hz), 2.13-2.03 (1H, m), 1.86-1.79 (1H, m), 1.32 (3H, t, J=7 Hz).

Example 77

Ethyl 8-[N-(2,4-difluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-276)



White powder (yield: 74%)

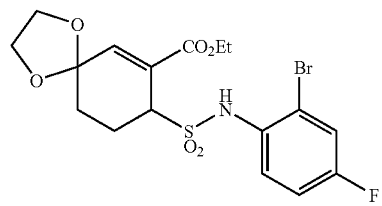
Melting point: 128-131° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.64-7.57 (1H, m), 6.97 (1H, brs), 6.93-6.86 (2H, m), 6.84 (1H, t, J=1 Hz), 4.36 (1H, dd, J=6 Hz, 2 Hz), 4.28-4.02 (5H, m), 3.95-3.90 (1H, m), 2.53-2.46 (1H, m), 2.40 (1H, td, J=1-4 Hz, 4 Hz), 2.21-2.10 (1H, m), 1.88-1.81 (1H, m), 1.29 (3H, t, J=7 Hz).

Example 78

Ethyl 8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1550)



Pale yellow powder (yield: 48%)

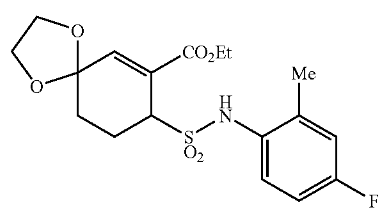
Melting point: 106-111° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.68 (1H, dd, J=9 Hz, 5 Hz), 7.32 (1H, dd, J=8 Hz, 3 Hz), 7.10-7.04 (1H, m), 6.94 (1H, s), 6.82 (1H, t, J=1 Hz), 4.46-4.43 (1H, m), 4.26-4.01 (5H, m), 3.95-3.89 (1H, m), 2.57-2.47 (2H, m), 2.24-2.13 (1H, m), 1.87-1.81 (1H, m), 1.26 (3H, t, J=7 Hz).

Example 79

Ethyl 8-[N-(4-fluoro-2-methylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2357)



White powder (yield: 79%)

Melting point: 103-105° C.

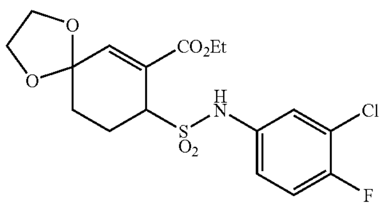
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, dd, J=9 Hz, 5 Hz), 6.96-6.85 (3H, m), 6.64 (1H, brs), 4.39 (1H, dd, J=6 Hz, 3 Hz), 4.27-4.18 (2H, m), 4.14-

4.02 (3H, m), 3.96-3.89 (1H, m), 2.52-2.45 (1H, m), 2.40-2.31 (4H, m), 2.18-2.08 (1H, m), 1.87-1.80 (1H, m), 1.29 (3H, t, J=7 Hz).

Example 80

Ethyl 8-[N-(3-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2364)



Pale brown powder (yield: 81%)

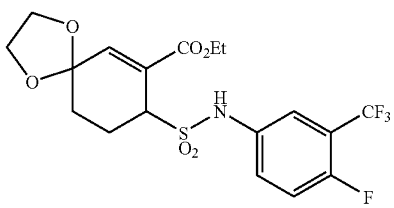
Melting point: 111-118° C.

[1]H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.47 (1H, dd, J=6 Hz, 3 Hz), 7.29-7.25 (1H, m), 7.15-7.09 (2H, m), 6.88 (1H, s), 4.28 (2H, q, J=7 Hz), 4.21-4.18 (1H, m), 4.14-4.02 (3H, m), 3.96-3.89 (1H, m), 2.49-2.41 (1H, m), 2.25 (1H, td, J=14 Hz, 3 Hz), 2.12-2.01 (1H, m), 1.89-1.82 (1H, m), 1.34 (3H, t, J=7 Hz).

Example 81

Ethyl 8-[N-(4-fluoro-3-trifluoromethylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2371)



White powder (yield: 78%)

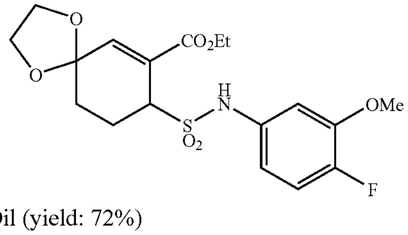
Melting point: 109-111° C.

[1]H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.64-7.57 (2H, m), 7.27-7.17 (2H, m), 6.89 (1H, s), 4.28 (2H, q, J=7 Hz), 4.19-4.16 (1H, m), 4.14-4.03 (3H, m), 3.96-3.89 (1H, m), 2.49-2.42 (1H, m), 2.26 (1H, td, J=14 Hz, 3 Hz), 2.13-2.03 (1H, m), 1.89-1.83 (1H, m), 1.34 (3H, t, J=7 Hz).

Example 82

Ethyl 8-[N-(4-fluoro-3-methoxy phenyl)sulfamoyl]-1,4-dioxaspiro[4,5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2378)



Oil (yield: 72%)

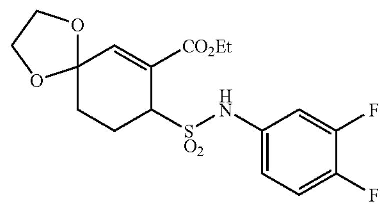
[1]H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.09 (1H, dd, J=7 Hz, 2 Hz), 7.03 (1H, dd, J=11 Hz, 9 Hz), 6.96 (1H, brs), 6.88-6.83 (2H, m), 4.30-4.23 (3H, m), 4.14-

4.02 (3H, m), 3.95-3.89 (4H, m), 2.46-2.38 (1H, m), 2.27 (1H, td, J=14 Hz, 3 Hz), 2.10-2.00 (1H, m), 1.88-1.81 (1H, m), 1.33 (3H, t, J=7 Hz).

Example 83

Ethyl 8-[N-(3,4-difluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2385)



Pale brown powder (yield: 94%)

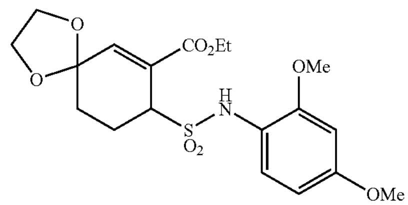
Melting point: 118-121° C.

[1]H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.33-7.26 (1H, m), 7.18-7.06 (3H, m), 6.89 (1H, s), 4.28 (2H, q, J=7 Hz), 4.19 (1H, dd, J=5 Hz, 3 Hz), 4.14-4.02 (3H, m), 3.96-3.89 (1H, m), 2.48-2.41 (1H, m), 2.25 (1H, td, J=14 Hz, 3 Hz), 2.11-2.01 (1H, m), 1.89-1.82 (1H, m), 1.34 (3H, t, J=7 Hz).

Example 84

Ethyl 8-[N-(2,4-dimethoxyphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2392)



White powder (yield: 49%)

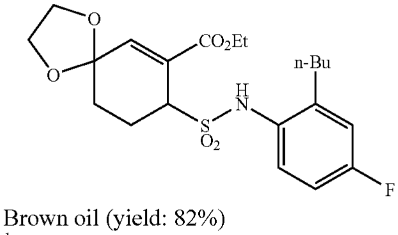
Melting point: 118-121° C.

[1]H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.47-7.45 (1H, m), 6.78 (2H, d, J=9.8 Hz), 6.50-6.47 (2H, m), 4.38 (1H, d, J=4.7 Hz), 4.21-3.80 (12H, m), 2.54 (1H, dt, J=14.2 Hz, 7.2 Hz), 2.45-2.38 (1H, m), 2.14-2.08 (1H, m), 1.81-1.76 (1H, m), 1.25 (3H, t, J=7.0 Hz).

Example 85

Ethyl 8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-628)



Brown oil (yield: 82%)

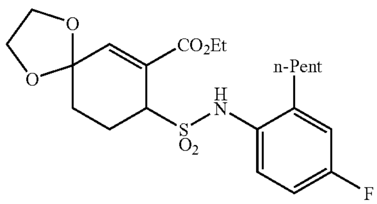
[1]H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, dd, J=9 Hz, 5 Hz), 6.94 (1H, dd, J=10 Hz, 3 Hz), 6.92-6.86 (2H, m), 6.60 (1H, s), 4.41 (1H, dd, J=6 Hz, 2 Hz),

4.28-4.18 (2H, m), 4.14-4.02 (3H, m), 3.96-3.89 (1H, m), 2.75-2.63 (2H, m), 2.52-2.45 (1H, m), 2.37 (1H, dt, J=14 Hz, 3 Hz), 2.18-2.08 (1H, m), 1.87-1.80 (1H, m), 1.63-1.52 (2H, m), 1.44-1.35 (2H, m), 1.29 (3H, t, J=7 Hz), 0.95 (3H, t, J=8 Hz).

Example 86

Ethyl 8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1726)



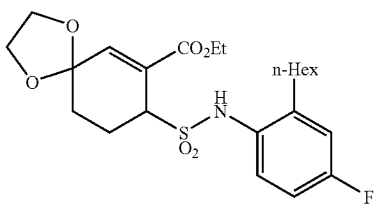
Brown oil (yield: 78%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, dd, J=9 Hz, 5 Hz), 6.94 (1H, dd, J=10 Hz, 3 Hz), 6.92-6.85 (2H, m), 6.61 (1H, s), 4.40 (1H, dd, J=6 Hz, 2 Hz), 4.27-4.18 (2H, m), 4.14-4.02 (3H, m), 3.95-3.90 (1H, m), 2.76-2.61 (2H, m), 2.52-2.45 (1H, m), 2.37 (1H, dt, J=14 Hz, 3 Hz), 2.18-2.09 (1H, m), 1.87-1.81 (1H, m), 1.65-1.52 (2H, m), 1.39-1.32 (4H, m), 1.30 (3H, t, J=7 Hz), 0.90 (3H, t, J=7 Hz).

Example 87

Ethyl 8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-804)



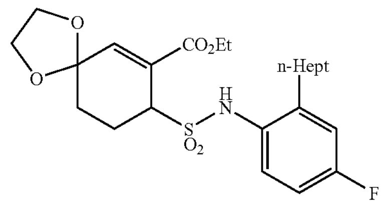
Pale brown oil (yield: 58%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, dd, J=9 Hz, 5 Hz), 6.96-6.85 (3H, m), 6.61 (1H, s), 4.40 (1H, dd, J=6 Hz, 2 Hz), 4.28-4.18 (2H, m), 4.14-4.02 (3H, m), 3.95-3.89 (1H, m), 2.76-2.61 (2H, m), 2.52-2.45 (1H, m), 2.37 (1H, td, J=14 Hz, 3 Hz), 2.18-2.08 (1H, m), 1.87-1.81 (1H, m), 1.63-1.52 (2H, m), 1.42-1.25 (9H, m), 0.91-0.85 (3H, m).

Example 88

Ethyl 8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-980)



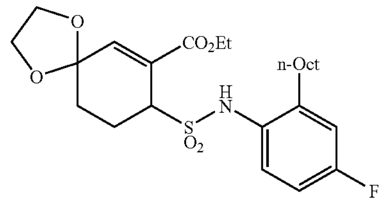
Pale yellow oil (yield: 85%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, dd, J=9 Hz, 5 Hz), 6.96-6.87 (3H, m), 6.63 (1H, s), 4.41 (1H, dd, J=6 Hz, 2 Hz), 4.27-4.19 (2H, m), 4.14-3.91 (4H, m), 2.76-2.62 (2H, m), 2.52-2.46 (1H, m), 2.37 (1H, dt, J=14 Hz, 3 Hz), 2.18-2.09 (1H, m), 1.84 (1H, dt, J=13 Hz, 4 Hz), 1.62-1.55 (2H, m), 1.40-1.24 (11H, m), 0.88 (3H, t, J=7 Hz).

Example 89

Ethyl 8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1902)



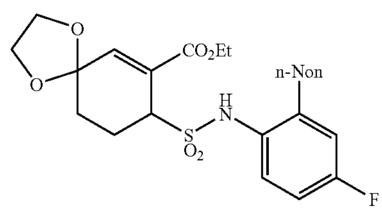
Pale yellow oil (yield: 72%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, dd, J=9 Hz, 5 Hz), 6.96-6.87 (3H, m), 6.62 (1H, s), 4.40 (1H, dd, J=6 Hz, 2 Hz), 4.27-4.19 (2H, m), 4.15-3.90 (4H, m), 2.74-2.62 (2H, m), 2.52-2.46 (1H, m), 2.37 (1H, dt, J=14 Hz, 3 Hz), 2.18-2.10 (1H, m), 1.86-1.81 (1H, m), 1.63-1.53 (2H, m), 1.40-1.24 (13H, m), 0.88 (3H, t, J=7 Hz).

Example 90

Ethyl 8-[N-(4-fluoro-2-nonylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2602)



Pale orange oil (yield: 82%)

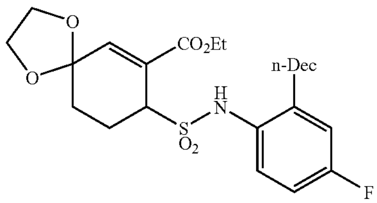
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.49 (1H, dd, J=9 Hz, 5 Hz), 6.94 (1H, dd, J=9 Hz, 3 Hz), 6.92-6.85 (2H, m), 6.62 (1H, s), 4.40 (1H, dd, J=6 Hz, 2 Hz), 4.28-4.17 (2H, m), 4.15-4.03 (3H, m), 3.95-3.90 (1H, m), 2.75-2.62 (2H, m), 2.52-2.45 (1H, m), 2.37 (1H, td, J=14 Hz,

3 Hz), 2.18-2.09 (1H, m), 1.86-1.81 (1H, m), 1.63-1.53 (2H, m), 1.39-1.22 (15H, m), 0.88 (3H, t, J=7 Hz).

Example 91

Ethyl 8-[N-(2-decyl-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2616)



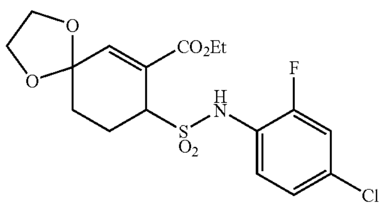
Pale yellow oil (yield: 83%)

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.49 (1H, dd, J=9 Hz, 5 Hz), 6.94 (1H, dd, J=9 Hz, 3 Hz), 6.92-6.85 (2H, m), 6.62 (1H, s), 4.40 (1H, dd, J=5 Hz, 3 Hz), 4.28-4.17 (2H, m), 4.15-4.03 (3H, m), 3.95-3.90 (1H, m), 2.75-2.62 (2H, m), 2.51-2.45 (1H, m), 2.37 (1H, td, J=14 Hz, 3 Hz), 2.18-2.09 (1H, m), 1.86-1.81 (1H, m), 1.63-1.53 (2H, m), 1.39-1.22 (17H, m), 0.88 (3H, t, J=7 Hz).

Example 92

Ethyl 8-[N-(4-chloro-2-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2399)



White powder (yield: 65%)

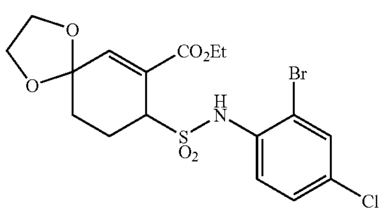
Melting point: 130-133° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.62-7.56 (1H, m), 7.18-7.11 (2H, m), 7.02 (1H, s), 6.84 (1H, t, J=1 Hz), 4.37 (1H, dd, J=6 Hz, 2 Hz), 4.25-4.02 (5H, m), 3.96-3.89 (1H, m), 2.55-2.48 (1H, m), 2.42 (1H, td, J=14 Hz, 4 Hz), 2.21-2.11 (1H, m), 1.88-1.82 (1H, m), 1.29 (3H, t, J=7 Hz).

Example 93

Ethyl 8-[N-(2-bromo-4-chlorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2406)



Pale brown powder (yield: 51%)

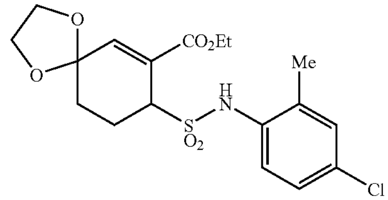
Melting point: 100-110° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.64 (1H, d, J=9 Hz), 7.56 (1H, d, J=3 Hz), 7.31 (1H, dd, J=9 Hz, 3 Hz), 7.02 (1H, s), 6.83 (1H, t, J=1 Hz), 4.47-4.43 (1H, m), 4.23-4.02 (5H, m), 3.95-3.89 (1H, m), 2.58-2.48 (2H, m), 2.24-2.14 (1H, m), 1.89-1.82 (1H, m), 1.26 (3H, t, J=7 Hz).

Example 94

Ethyl 8-[N-(4-chloro-2-methylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2413)



White powder (yield: 74%)

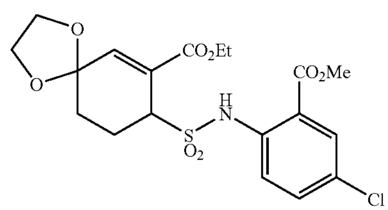
Melting point: 123-126° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, d, J=9 Hz), 4.21-4.15 (2H, m), 6.86 (1H, t, J=1 Hz), 6.65 (1H, s), 4.38 (1H, dd, J=6 Hz, 3 Hz), 4.24-4.15 (2H, m), 4.14-4.02 (3H, m), 3.96-3.89 (1H, m), 2.54-2.47 (1H, m), 2.41-2.32 (4H, m), 2.19-2.09 (1H, m), 1.88-1.82 (1H, m), 1.29 (3H, t, J=7 Hz).

Example 95

Ethyl 8-[N-(4-chloro-2-methoxycarbonylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2420)



White powder (yield: 46%)

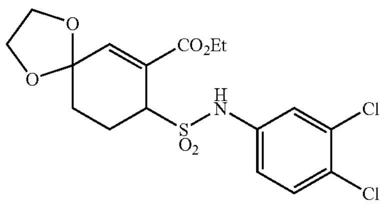
Melting point: 131-134° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

10.48 (1H, s), 8.00 (1H, d, J=3 Hz), 7.79 (1H, d, J=9 Hz), 7.50 (1H, dd, J=9 Hz, 3 Hz), 6.80 (1H, t, J=1 Hz), 4.47 (1H, dd, J=6 Hz, 2 Hz), 4.14-4.01 (5H, m), 3.95-3.88 (4H, m), 2.66-2.50 (2H, m), 2.22-2.11 (1H, m), 1.88-1.81 (1H, m), 1.25 (3H, t, J=7 Hz).

Example 96

Ethyl 8-[N-(3,4-dichlorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2427)



White powder (yield: 66%)

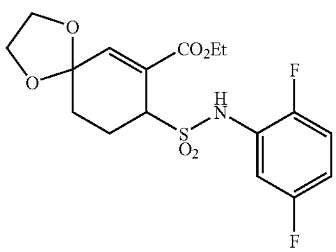
Melting point: 163-164° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, d, J=2 Hz), 7.41 (1H, d, J=9 Hz), 7.23 (1H, dd, J=9 Hz, 3 Hz), 7.16 (1H, s), 6.88 (1H, t, J=1 Hz), 4.27 (2H, q, J=7 Hz), 4.21 (1H, q, J=3 Hz), 4.14-4.02 (3H, m), 3.96-3.88 (1H, m), 2.50-2.43 (1H, m), 2.27 (1H, td, J=14 Hz, 3 Hz), 2.13-2.03 (1H, m), 1.89-1.82 (1H, m), 1.33 (3H, t, J=7 Hz).

Example 97

Ethyl 8-[N-(2,5-difluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2434)



Pale brown powder (yield: 61%)

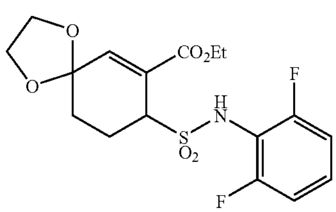
Melting point: 125-128° C.

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.45-7.41 (1H, m), 7.09-7.00 (2H, m), 6.86 (1H, s), 6.80-6.74 (1H, m), 4.41 (1H, dd, J=6 Hz, 2 Hz), 4.26-4.02 (5H, m), 3.95-3.90 (1H, m), 2.58-2.52 (1H, m), 2.44 (1H, td, J=14 Hz, 3 Hz), 2.23-2.14 (1H, m), 1.89-1.84 (1H, m), 1.28 (3H, t, J=7 Hz).

Example 98

Ethyl 8-[N-(2,6-difluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2441)



White powder (yield: 56%)

Melting point: 129-131° C.

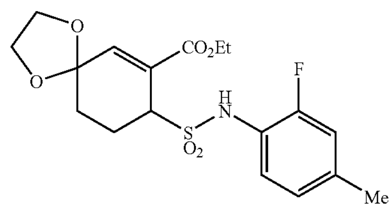
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.25-7.18 (1H, m), 7.01-6.95 (2H, m), 6.89-6.87 (2H, m), 4.64 (1H, dd, J=5 Hz, 2 Hz), 4.31-4.21 (2H, m), 4.15-4.03

(3H, m), 3.96-3.91 (1H, m), 2.63-2.57 (1H, m), 2.36 (1H, td, J=14 Hz, 3 Hz), 2.26-2.17 (1H, m), 1.87-1.82 (1H, m), 1.29 (3H, t, J=7 Hz).

Example 99

Ethyl 8-[N-(2-fluoro-4-methylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2448)



White powder (yield: 69%)

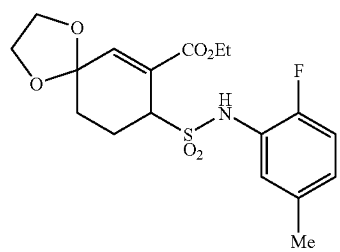
Melting point: 136-138° C.

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.49 (1H, t, J=9 Hz), 6.95-6.92 (2H, m), 6.86 (1H, d, J=2 Hz), 6.83 (1H, s), 4.40-4.37 (1H, m), 4.26-4.15 (2H, m), 4.13-4.01 (3H, m), 3.94-3.89 (1H, m), 2.51-2.40 (2H, m), 2.32 (3H, s), 2.18-2.09 (1H, m), 1.86-1.81 (1H, m), 1.27 (3H, t, J=7 Hz).

Example 100

Ethyl 8-[N-(2-fluoro-5-methylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2455)



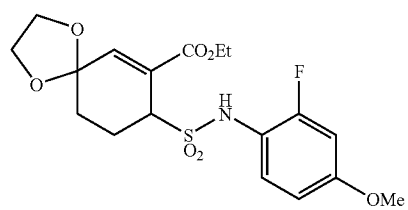
Oil (yield: 63%)

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.43 (1H, dd, J=8 Hz, 2 Hz), 6.98 (1H, dd, J=10 Hz, 8 Hz), 6.91-6.87 (2H, m), 6.83 (1H, t, J=1 Hz), 4.42 (1H, dd, J=6 Hz, 2 Hz), 4.26-4.02 (5H, m), 3.95-3.89 (1H, m), 2.54-2.42 (2H, m), 2.20-2.12 (1H, m), 1.87-1.82 (1H, m), 1.27 (3H, t, J=7 Hz).

Example 101

Ethyl 8-[N-(2-fluoro-4-methoxyphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2462)



Pale brown powder (yield: 57%)

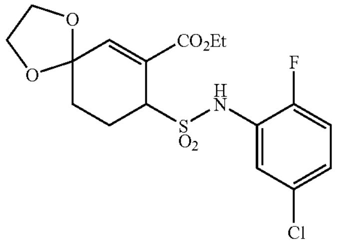
Melting point: 167-169° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.50 (1H, t, J=9 Hz), 6.82 (1H, t, J=1 Hz), 6.79 (1H, brs), 6.71-6.67 (2H, m), 4.38-4.35 (1H, m), 4.28-4.19 (2H, m), 4.14-4.01 (3H, m), 3.95-3.88 (1H, m), 3.79 (3H, s), 2.49-2.36 (2H, m), 2.18-2.08 (1H, m), 1.86-1.79 (1H, m), 1.29 (3H, t, J=7 Hz).

Example 102

Ethyl 8-[N-(5-chloro-2-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2469)



White powder (yield: 55%)

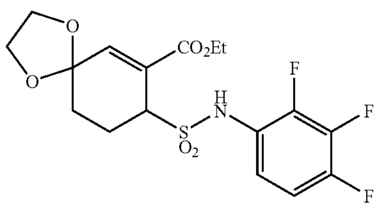
Melting point: 88-90° C.

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.68-7.65 (1H, m), 7.07-7.01 (3H, m), 6.86 (1H, s), 4.40 (1H, dd, J=6 Hz, 2 Hz), 4.27-4.15 (2H, m), 4.14-4.03 (3H, m), 3.96-3.90 (1H, m), 2.58-2.52 (1H, m), 2.43 (1H, td, J=14 Hz, 3 Hz), 2.23-2.15 (1H, m), 1.89-1.84 (1H, m), 1.29 (3H, t, J=7 Hz).

Example 103

Ethyl 8-[N-(2,3,4-trifluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2476)



White powder (yield: 71%)

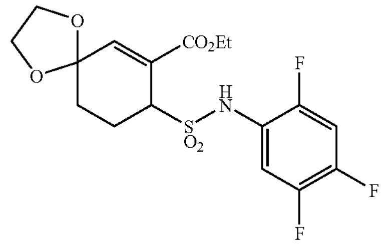
Melting point: 149-152° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.41-7.34 (1H, m), 7.14 (1H, brs), 7.02-6.93 (1H, m), 6.85 (1H, t, J=1 Hz), 4.36 (1H, dd, J=6 Hz, 2 Hz), 4.28-4.20 (2H, m), 4.14-4.02 (3H, m), 3.96-3.90 (1H, m), 2.55-2.46 (1H, m), 2.38 (1H, td, J=14 Hz, 4 Hz), 2.22-2.12 (1H, m), 1.89-1.82 (1H, m), 1.31 (3H, t, J=7 Hz).

Example 104

Ethyl 8-[N-(2,4,5-trifluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2483)



White powder (yield: 72%)

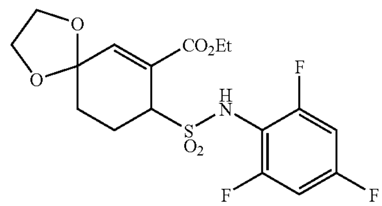
Melting point: 104-107° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.60-7.52 (1H, m), 7.05-6.97 (2H, m), 6.86 (1H, t, J=1 Hz), 4.35 (1H, dd, J=6 Hz, 2 Hz), 4.28-4.19 (2H, m), 4.15-4.02 (3H, m), 3.96-3.90 (1H, m), 2.56-2.49 (1H, m), 2.38 (1H, td, J=14 Hz, 4 Hz), 2.23-2.12 (1H, m), 1.90-1.83 (1H, m), 1.30 (3H, t, J=7 Hz).

Example 105

Ethyl 8-[N-(2,4,6-trifluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2490)



White powder (yield: 61%)

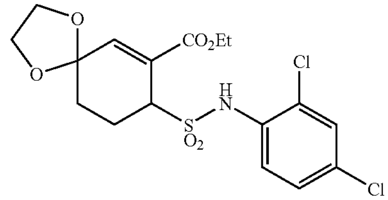
Melting point: 131-133° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

6.91 (1H, s), 6.88 (1H, t, J=1 Hz), 6.80-6.72 (2H, m), 4.55 (1H, dd, J=6 Hz, 3 Hz), 4.31-4.23 (2H, m), 4.14-4.03 (3H, m), 3.96-3.90 (1H, m), 2.62-2.55 (1H, m), 2.32 (1H, td, J=14 Hz, 3 Hz), 2.25-2.15 (1H, m), 1.88-1.81 (1H, m), 1.31 (3H, t, J=7 Hz).

Example 106

Ethyl 8-[N-(2,4-dichlorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2497)



Pale brown powder (yield: 67%)

Melting point: 109-111° C.

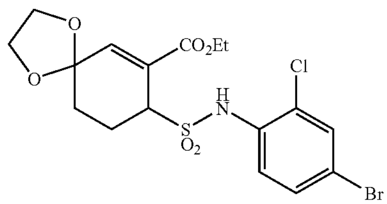
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.65 (1H, d, J=9 Hz), 7.41 (1H, d, J=2 Hz), 7.28-7.24 (1H, m), 7.07 (1H, s), 6.83 (1H, s), 4.46-4.42 (1H, m), 4.24-4.02

(5H, m), 3.98-3.89 (1H, m), 2.56-2.46 (2H, m), 2.24-2.13 (1H, m), 1.89-1.82 (1H, m), 1.26 (3H, t, J=7 Hz).

Example 107

Ethyl 8-[N-(4-bromo-2-chlorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2504)



White powder (yield: 74%)

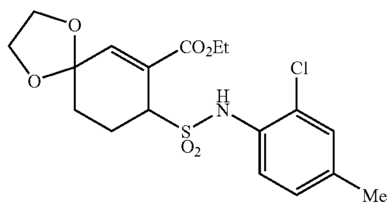
Melting point: 102-107° C.

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.59 (1H, d, J=9 Hz), 7.55 (1H, d, J=2 Hz), 7.40 (1H, dd, J=9 Hz, 2 Hz), 7.08 (1H, s), 6.83 (1H, s), 4.44 (1H, d, J=5 Hz), 4.23-4.02 (5H, m), 3.95-3.89 (1H, m), 2.55-2.47 (2H, m), 2.23-2.14 (1H, m), 1.89-1.83 (1H, m), 1.26 (3H, t, J=7 Hz).

Example 108

Ethyl 8-[N-(2-chloro-4-methylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-452)



Pale brown powder (yield: 69%)

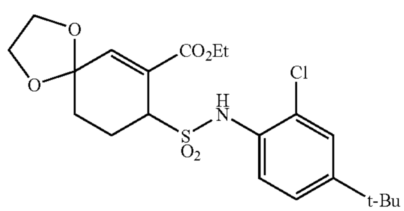
Melting point: 130-135° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.57 (1H, d, J=9 Hz), 7.20 (1H, d, J=2 Hz), 7.10-7.06 (1H, m), 6.97 (1H, s), 6.81 (1H, d, J=1 Hz), 4.44 (1H, d, J=5 Hz), 4.25-4.00 (5H, m), 3.95-3.87 (1H, m), 2.59-2.45 (2H, m), 2.31 (3H, s), 2.22-2.10 (1H, m), 1.87-1.79 (1H, m), 1.25 (3H, t, J=7 Hz).

Example 109

Ethyl 8-[N-(4-t-butyl-2-chlorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2511)



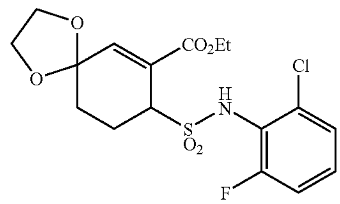
Amorphous substance (yield: 49%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.61 (1H, d, J=9 Hz), 7.38 (1H, d, J=2 Hz), 7.29 (1H, dd, J=9 Hz, 2 Hz), 7.00 (1H, s), 6.82 (1H, s), 4.46 (1H, d, J=4 Hz), 4.23-4.01 (5H, m), 3.95-3.88 (1H, m), 2.59-2.47 (2H, m), 2.23-2.12 (1H, m), 1.87-1.80 (1H, m), 1.29 (9H, s), 1.25-1.21 (3H, m).

Example 110

Ethyl 8-[N-(2-chloro-6-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2518)



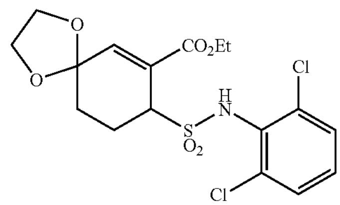
Amorphous substance (yield: 62%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.27-7.24 (1H, m), 7.21-7.15 (1H, m), 7.12-7.06 (1H, m), 6.98 (1H, s), 6.86 (1H, s), 4.77-4.74 (1H, m), 4.30-4.21 (2H, m), 4.15-4.03 (3H, m), 3.96-3.90 (1H, m), 2.67-2.60 (1H, m), 2.38 (1H, td, J=14 Hz, 3 Hz), 2.28-2.17 (1H, m), 1.88-1.81 (1H, m), 1.29 (3H, t, J=7 Hz).

Example 111

Ethyl 8-[N-(2,6-dichlorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2525)



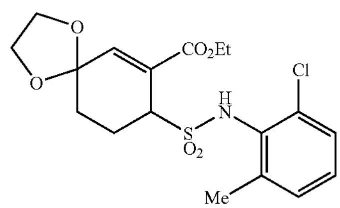
Amorphous substance (yield: 24%)

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.39 (1H, s), 7.38 (1H, s), 7.27 (1H, s), 7.17 (1H, t, J=8 Hz), 6.87 (1H, s), 4.88 (1H, dd, J=5 Hz, 3 Hz), 4.29 (2H, q, J=7 Hz), 4.15-4.03 (3H, m), 3.96-3.91 (1H, m), 2.68-2.62 (1H, m), 2.31 (1H, td, J=14 Hz, 3 Hz), 2.26-2.18 (1H, m), 1.88-1.82 (1H, m), 1.31 (3H, t, J=7 Hz).

Example 112

Ethyl 8-[N-(2-chloro-6-methylphenyl) sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1462)



Amorphous substance (yield: 55%)

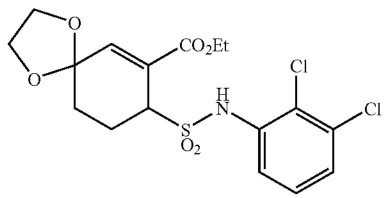
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.29-7.23 (1H, m), 7.20-7.09 (3H, m), 6.84 (1H, t, J=1 Hz), 4.80-4.77 (1H, m), 4.30-4.20 (2H, m), 4.13-4.00 (3H, m),

3.95-3.89 (1H, m), 2.58-2.46 (4H, m), 2.33 (1H, td, J=14 Hz, 3 Hz), 2.25-2.14 (1H, m), 1.85-1.78 (1H, m), 1.28 (3H, t, J=7 Hz).

Example 113

Ethyl 8-[N-(2,3-dichlorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2532)



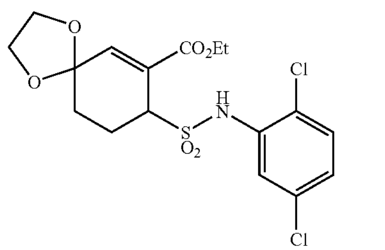
Amorphous substance (yield: 70%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.56-7.61 (1H, m), 7.26-7.19 (3H, m), 5.83 (1H, s), 4.46 (1H, d, J=5 Hz), 4.22-4.01 (5H, m), 3.95-3.89 (1H, m), 2.57-2.48 (2H, m), 2.25-2.14 (1H, m), 1.89-1.82 (1H, m), 1.25 (3H, t, J=7 Hz).

Example 114

Ethyl 8-[N-(2,5-dichlorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2539)



White powder (yield: 78%)

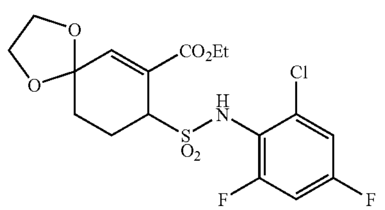
Melting point: 120-124° C.

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.72 (1H, d, J=2 Hz), 7.31 (1H, d, J=9 Hz), 7.11 (1H, s), 7.05 (1H, dd, J=9 Hz, 2 Hz), 6.86 (1H, s), 4.46 (1H, dd, J=6 Hz, 2 Hz), 4.25-4.03 (5H, m), 3.95-3.90 (1H, m), 2.58-2.48 (2H, m), 2.26-2.17 (1H, m), 1.90-1.84 (1H, m), 1.26 (3H, t, J=7 Hz).

Example 115

Ethyl 8-[N-(2-chloro-4,6-difluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2546)



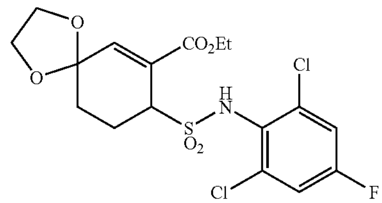
Oil (yield: 29%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.07-7.03 (1H, m), 6.99 (1H, s), 6.91-6.83 (2H, m), 4.67 (1H, dd, J=5 Hz, 3 Hz), 4.31-4.23 (2H, m), 4.14-4.03 (3H, m), 3.97-3.90 (1H, m), 2.65-2.57 (1H, m), 2.34 (1H, td, J=14 Hz, 3 Hz), 2.27-2.17 (1H, m), 1.88-1.81 (1H, m), 1.31 (3H, t, J=7 Hz).

Example 116

Ethyl 8-[N-(2,6-dichloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2553)



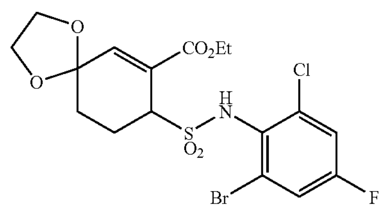
Amorphous substance (yield: 39%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.22 (1H, s), 7.17 (2H, d, J=7 Hz), 6.88 (1H, t, J=1 Hz), 4.84-4.81 (1H, m), 4.29 (2H, q, J=7 Hz), 4.14-4.03 (3H, m), 3.97-3.90 (1H, m), 2.67-2.60 (1H, m), 2.34-2.17 (2H, m), 1.88-1.81 (1H, m), 1.33 (3H, t, J=7 Hz).

Example 117

Ethyl 8-[N-(2-bromo-6-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2560)



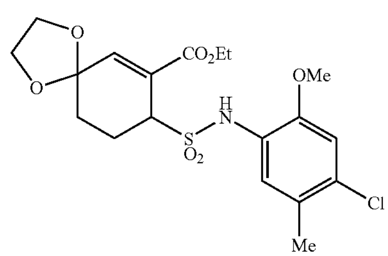
Amorphous substance (yield: 46%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.35 (1H, dd, J=7.5 Hz, 2.8 Hz), 7.24-7.21 (2H, m), 7.24 (1H, s), 4.90 (1H, d, J=5.1 Hz), 4.30 (2H, q, J=7.2 Hz), 4.14-3.92 (4H, m), 2.67-2.62 (1H, m), 2.33-2.18 (2H, m), 1.88-1.84 (1H, m), 1.33 (3H, t, J=6.6 Hz).

Example 118

Ethyl 8-[N-(4-chloro-2-methoxy-5-methylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2567)



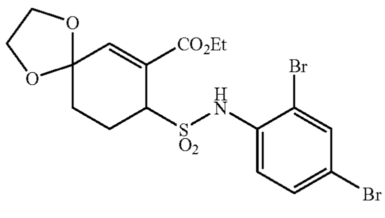
White powder (yield: 54%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.43 (1H, s), 6.96 (1H, s), 6.87 (1H, s), 6.78 (1H, t, J=1 Hz), 4.41 (1H, dd, J=6 Hz, 2 Hz), 4.20-4.00 (5H, m), 3.94-3.88 (1H, m), 3.85 (3H, s), 2.58-2.43 (2H, m), 2.31 (3H, s), 2.20-2.08 (1H, m), 1.85-1.78 (1H, m), 1.25 (3H, t, J=7 Hz).

Example 119

Ethyl 8-[N-(2,4-dibromophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2574)



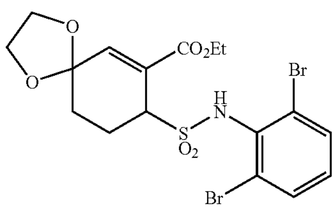
Oil (yield: 56%)

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.70 (1H, d, J=2 Hz), 7.59 (1H, d, J=9 Hz), 7.44 (1H, dd, J=9 Hz, 2 Hz), 7.02 (1H, s), 6.83 (1H, s), 4.47-4.44 (1H, m), 4.23-4.02 (5H, m), 3.95-3.90 (1H, m), 2.57-2.49 (2H, m), 2.23-2.15 (1H, m), 1.88-1.83 (1H, m), 1.26 (3H, t, J=7 Hz).

Example 120

Ethyl 8-[N-(2,6-dibromophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2581)



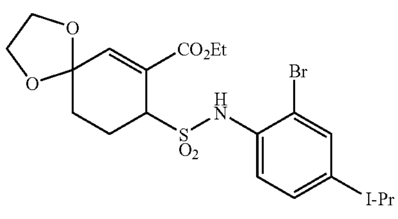
Amorphous substance (yield: 41%)

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.61 (2H, d, J=8 Hz), 7.26 (1H, brs), 7.02 (1H, t, J=8 Hz), 6.88 (1H, s), 5.02-5.00 (1H, m), 4.29 (2H, q, J=7 Hz), 4.15-3.91 (4H, m), 2.70-2.64 (1H, m), 2.33-2.19 (2H, m), 1.87-1.83 (1H, m), 1.32 (3H, t, J=7 Hz).

Example 121

Ethyl 8-[N-(2-bromo-4-isopropylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2588)



White powder (yield: 51%)

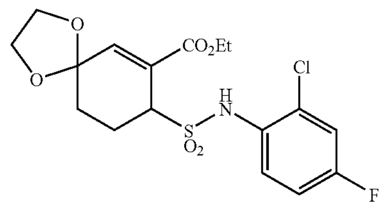
Melting point: 130-134° C.

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.60 (1H, d, J=8 Hz), 7.40 (1H, d, J=2 Hz), 7.18 (1H, dd, J=8 Hz, 2 Hz), 6.94 (1H, s), 6.82 (1H, s), 4.48-4.46 (1H, m), 4.24-4.01 (5H, m), 3.94-3.88 (1H, m), 2.89-2.83 (1H, m), 2.60-2.47 (2H, m), 2.22-2.13 (1H, m), 1.86-1.81 (1H, m), 1.25-1.21 (9H, m).

Example 122

Ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-364)



Ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 1 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as a white powder. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 1:1
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 6.1 minutes
	high polarity compound (second peak): 10.5 minutes

(Low Polarity Compound, First Peak)

Melting point: 116-117° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.68 (1H, dd, J=9.2 Hz, 5.3 Hz), 7.17 (1H, dd, J=7.8 Hz, 2.7 Hz), 7.05-7.00 (2H, m), 6.83 (1H, s), 4.43 (1H, d, J=5.4 Hz), 4.26-3.90 (6H, m), 2.55-2.47 (2H, m), 4.15-2.47 (1H, m), 4.02-2.13 (1H, m), 1.27 (3H, t, J=7.0 Hz).

(High Polarity Compound, Second Peak)

Melting point: 116-117° C.

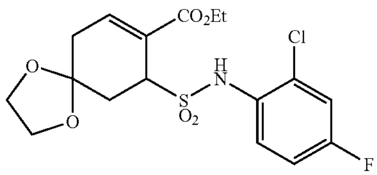
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.68 (1H, dd, J=9.0 Hz, 5.5 Hz), 7.17 (1H, dd, J=8.0 Hz, 2.9 Hz), 7.06-7.00 (2H, m), 6.84 (1H, s), 4.43 (1H, d, J=5.4 Hz),

4.26-3.90 (6H, m), 2.55-2.47 (2H, m), 1.13-2.23 (1H, m), 1.87-1.83 (1H, m), 1.27 (3H, t, J=6.6 Hz).

Example 123

Ethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-7-ene-8-carboxylate



(123a) Ethyl 7-trifluoromethanesulfonyloxy-1,4-dioxaspiro[4.5]dec-7-ene-8-carboxylate

Following the process described in Example (30e), ethyl 7-oxo-1,4-dioxaspiro[4.5]decane-8-carboxylate [compound disclosed as Compound 292c in US Patent application No. US2004/259914 A1] was used in place of ethyl 8-oxo-1-oxaspiro[4.5]decane-7-carboxylate to give the title compound as a white powder (yield: 96%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.28 (2H, q, J=7 Hz), 4.04-3.96 (4H, m), 2.65-2.61 (4H, m), 1.82-1.78 (2H, m), 1.32 (3H, t, J=7 Hz).

(123b) Ethyl 7-acetylsulfanyl-1,4-dioxaspiro[4.5]dec-7-ene-8-carboxylate

Following the process described in Example (1a), ethyl 7-trifluoromethanesulfonyloxy-1,4-dioxaspiro[4.5]dec-7-ene-8-carboxylate obtained in (123a) was used in place of ethyl 8-trifluoromethanesulfonyloxy-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate to obtain the title compound as a pale brown oil (yield: 83%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.21 (2H, q, 7 Hz), 4.04-3.96 (4H, m), 2.72-2.65 (4H, m), 2.32 (3H, s), 1.85 (2H, t, J=7 Hz), 1.29 (3H, t, J=7 Hz).

(123c) Ethyl 7-mercapto-1,4-dioxaspiro[4.5]dec-7-ene-8-carboxylate

Following the process described in Example (1b), ethyl 7-acetylsulfanyl-1,4-dioxaspiro[4.5]dec-7-ene-8-carboxylate obtained in (123b) was used in place of ethyl 8-acetylsulfanyl-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate to give the title compound as a pale brown powder (yield: 85%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.22 (2H, q, 7 Hz), 4.20 (1H, s), 4.02-3.95 (4H, m), 2.69-2.66 (2H, m), 2.61-2.56 (2H, m), 1.82-1.78 (2H, m), 1.30 (3H, t, J=7 Hz).

(123d) Ethyl 7-chlorosulfonyl-1,4-dioxaspiro[4.5]dec-7-ene-8-carboxylate

Following the process described in Example (1c), ethyl 7-mercapto-1,4-dioxaspiro[4.5]dec-7-ene-8-carboxylate obtained in (123c) was used in place of ethyl 8-mercapto-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate to give the title compound as a colorless oil (yield: 62%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.31 (2H, q, 7 Hz), 4.09-4.00 (4H, m), 2.82-2.73 (4H, m), 1.86 (2H, t, J=7 Hz), 1.35 (3H, t, J=7 Hz).

(123e) Ethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-7-ene-8-carboxylate

Following the process described in Example (1d), ethyl 7-chlorosulfonyl-1,4-dioxaspiro[4.5]dec-7-ene-8-carboxylate obtained in (123d) was used in place of ethyl 8-chlorosulfonyl-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate to give the title compound as a white powder (yield: 61%).

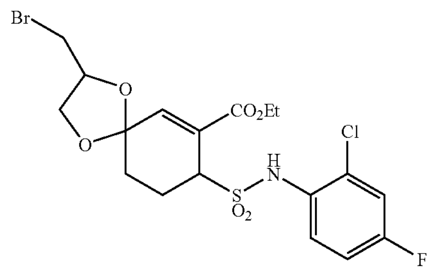
Melting point: 120-122° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.81 (1H, s), 7.66 (1H, dd, J=9 Hz, 5 Hz), 7.14-7.10 (2H, m), 6.98-6.92 (1H, m), 4.71-4.67 (1H, m), 4.22-3.96 (6H, m), 2.75-2.56 (3H, m), 2.08-2.02 (1H, m), 1.24 (3H, t, J=7 Hz).

Example 124

Ethyl 2-bromoethyl-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate



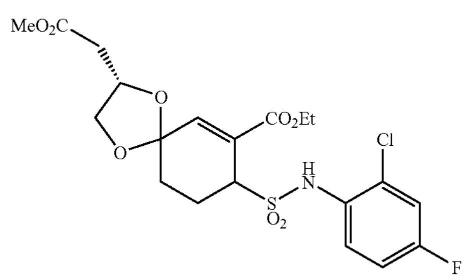
Following the process described in Example (17a), 1-bromo-2,3-bis[(trimethylsilyl)oxy]propane was used in place of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-D-threitol to give the title compound as a white amorphous substance (yield: 100%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.67 (1H, dd, J=9.2 and 5.3 Hz), 7.17 (1H, dd, J=7.8 and 2.8 Hz), 7.05-6.99 (2H, m), 6.86-6.77 (1H, m), 4.53-3.84 (6H, m), 3.53-3.31 (2H, m), 2.66-2.41 (2H, m), 2.24-2.12 (1H, m), 1.89-1.86 (1H, m), 1.28-1.24 (3H, m).

Example 125

Ethyl (2S)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-methoxycarbonylmethyl-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate



Following the process described in Example (17a), methyl (S)-3,4-bis[(trimethylsilyl)oxy]butyrate obtained in Refer-

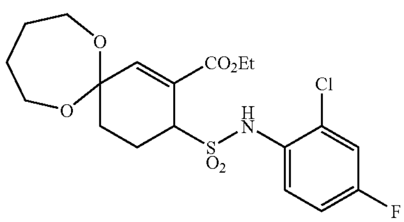
ence Example 20 was used in place of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-D-threitol to give the title compound as a colorless oil (yield: 96%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.67 (1H, dd, J=9.0 Hz, 5.4 Hz), 7.16 (1H, dd, J=7.9 Hz, 2.8 Hz), 7.05-6.98 (2H, m), 6.88-6.76 (1H, m), 4.63-4.58 (1H, m), 4.47-4.41 (1H, m), 4.32-4.10 (3H, m), 3.84-3.59 (4H, m), 2.85-2.39 (4H, m), 2.21-2.16 (1H, m), 1.89-1.80 (1H, m), 1.29-1.24 (3H, m).

Example 126

Ethyl 3-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-7,12-dioxaspiro[5.6]dodec-1-ene-2-carboxylate (Exemplified compound No. 1-366)



34 mg (0.61 mmol) of 1,4-butanediol was dissolved in 5 ml of dichloromethane, 0.32 ml (1.83 mmol) of isopropoxytrimethylsilane, and 200 mg (0.47 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-dimethoxy-1-cyclohexene-1-carboxylate obtained in Example (16a) and 4 μl (0.024 mmol) of trimethylsilyl trifluoromethanesulfonate were sequentially added thereto with stirring under ice-cooling, followed by stirring for 2 hours at the same temperature. Saturated aqueous sodium hydrogencarbonate was added to the reaction solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=3:1), and the resulting solid was further washed with hexane to give 6 mg of the title compound as a white powder (yield: 3%).

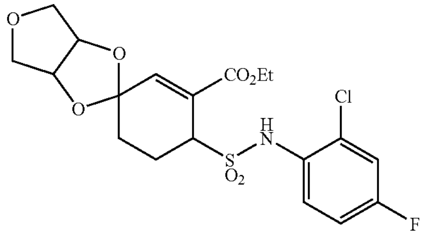
Melting point: 142-144° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.68 (1H, dd, J=9 Hz, 5 Hz), 7.16 (1H, dd, J=8 Hz, 3 Hz), 7.04 (1H, s), 7.03-6.98 (2H, m), 4.44-4.40 (1H, m), 4.27-4.11 (2H, m), 3.91-3.62 (4H, m), 2.46-2.38 (1H, m), 2.31-2.21 (1H, m), 2.17-1.94 (2H, m), 1.71-1.58 (4H, m), 1.27 (3H, t, J=7 Hz).

Example 127

Ethyl 4-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3a',4',6',6a'-tetrahydrospiro[cyclohex-2-ene-1,2'-furo[3.4-d][1.3]dioxol]-3-carboxylate (Exemplified compound No. 1-402)



Following the process described in Example 21, 1,4-anhydro-2,3-di-O-trimethylsilyl-meso-erythritol obtained in Reference Example 21 was used in place of 1,3,4,5,7-penta-O-trimethylsilyl-D-arabitol to give the title compound as a white powder (yield: 56%).

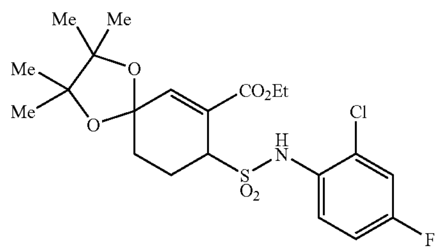
Melting point: 227-228° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$+CD_3OD) δ ppm:

7.61 (1H, dd, J=9 Hz, 5 Hz), 7.17 (1H, dd, J=8 Hz, 3 Hz), 7.07-6.97 (1H, m), 6.91 (1H, s), 4.93 (1H, dd, J=6 Hz, 4 Hz), 4.81 (1H, dd, J=6 Hz, 4 Hz), 4.39 (1H, d, J=5 Hz), 4.26-4.05 (3H, m), 4.01 (1H, d, J=11 Hz), 3.51-3.41 (2H, m), 2.54-2.34 (2H, m), 2.20-2.07 (1H, m), 1.90-1.79 (1H, m), 1.25 (3H, t, J=7 Hz).

Example 128

Ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,2,3,3-tetramethyl-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate



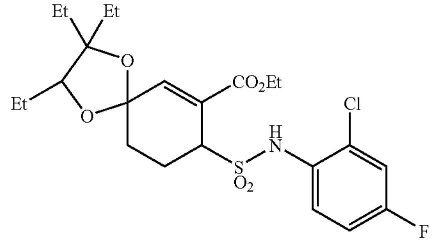
Following the process described in Example (17a), 2,3-dimethyl-2,3-bis[(trimethylsilyl)oxy]butane was used in place of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-D-threitol to give the title compound as a pale yellow oil (yield: 10%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.66 (1H, dd, J=8.8 Hz, 5.6 Hz), 7.16 (1H, dd, J=7.8 Hz, 2.7 Hz), 7.04-7.03 (1H, m), 6.89 (1H, s), 4.37 (1H, d, J=4.0 Hz), 4.25-4.10 (2H, m), 2.51-2.43 (2H, m), 2.24-2.14 (1H, m), 1.94-1.89 (1H, m), 1.31-1.23 (15H, m).

Example 129

Ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,2,3-triethyl-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate



Following the process described in Example (17a), 3-ethyl-3,4-bis[(trimethylsilyl)oxy]hexane obtained in Ref-

erence Example 22 was used in place of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-D-threitol to give the title compound as a white powder (yield: 88%).

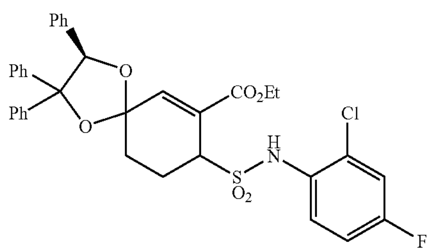
Melting point: 124-126° C.

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.69-7.66 (1H, m), 7.17-7.15 (1H, m), 7.04-7.00 (2H, m), 6.88-6.69 (1H, m), 4.40-4.39 (1H, m), 4.28-4.10 (2H, m), 3.90-3.68 (1H, m), 2.54-2.31 (2H, m), 2.25-2.12 (1H, m), 1.85-1.37 (7H, m), 1.29-1.24 (3H, m), 1.08-0.84 (9H, m).

Example 130

Ethyl (3R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,2,3-triphenyl-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate



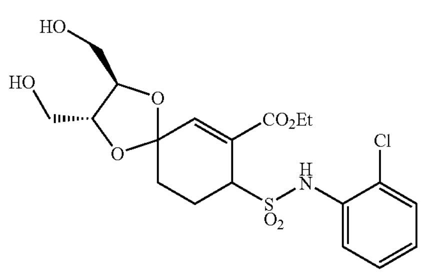
Following the process described in Example (17a), (R)-1,2-bis[(trimethylsilyl)oxy]-1,1,2-triphenylethane obtained in Reference Example 23 was used in place of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-D-threitol to give the title compound as a colorless oil (yield: 30%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.22-6.91 (20H, m), 5.99-5.76 (1H, m), 4.54-4.32 (1H, m), 4.34-4.08 (2H, m), 2.87-1.97 (4H, m), 1.36-1.14 (3H, m).

Example 131

Ethyl (2R,3R)-8-[N-(2-chlorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-206)



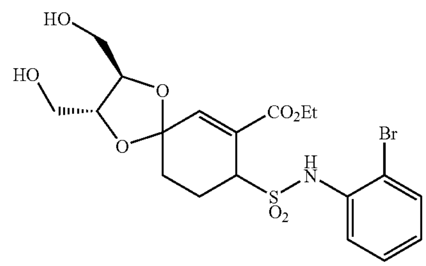
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2-chlorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 54 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 31%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.71-7.67 (1H, m), 7.41-7.38 (1H, m), 7.32-7.26 (1H, m), 7.14-7.06 (2H, m), 6.90 (0.5H, t, J=1 Hz), 6.84 (0.5H, t, J=1 Hz), 4.47 (1H, dd, J=6 Hz, 2 Hz), 4.26-4.07 (3.5H, m), 4.05-4.00 (0.5H, m), 3.94-3.80 (2H, m), 3.77-3.67 (2H, m), 2.64-2.47 (2H, m), 2.27-1.87 (4H, m), 1.27-1.22 (3H, m).

Example 132

Ethyl (2R,3R)-8-[N-(2-bromophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1392)



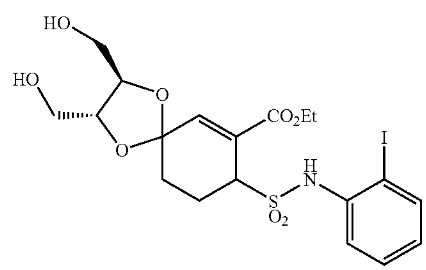
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2-bromophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 55 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 28%)

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.71-7.67 (1H, m), 7.56 (1H, d, J=8 Hz), 7.35-7.31 (1H, m), 7.07-6.98 (2H, m), 6.90 (0.5H, s), 6.84 (0.5H, s), 4.48 (1H, d, J=5 Hz), 4.25-4.08 (3.5H, m), 4.06-4.01 (0.5H, m), 3.94-3.80 (2H, m), 3.76-3.68 (2H, m), 2.65-2.48 (2H, m), 2.23-1.87 (4H, m), 1.27-1.22 (3H, m).

Example 133

Ethyl (2R,3R)-2,3-bis(hydroxymethyl)-8-[N-(2-iodophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2226)



Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2-iodophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 56 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 26%).

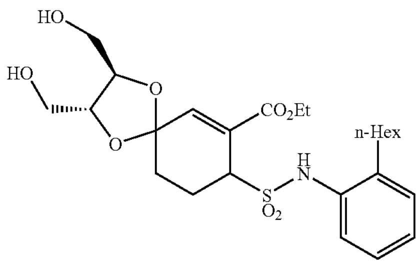
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.80 (1H, d, J=8 Hz), 7.68-7.63 (1H, m), 7.38-7.33 (1H, m), 6.90-6.83 (3H, m), 4.50-4.46 (1H, m), 4.27-4.09 (3.5H, m), 4.06-4.02 (0.5H, m), 3.94-3.80 (2H, m), 3.77-3.68 (2H,

m), 3.53 (1H, brs), 2.66-2.56 (1H, m), 2.55-2.49 (1H, m), 2.24-2.14 (1H, m), 2.00-1.85 (2H, m), 1.27-1.23 (3H, m).

Example 134

Ethyl (2R,3R)-8-[N-(2-hexylphenyl)sulfamoyl]-2,3-bis (hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-734)



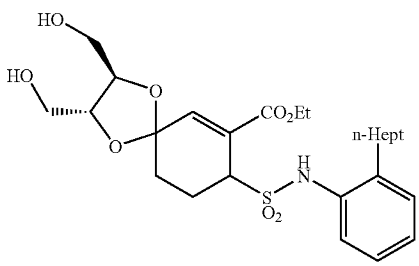
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2-hexylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 4 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as a colorless oil (yield: 28%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.54-7.50 (1H, m), 7.23-7.17 (2H, m), 7.15-7.09 (1H, m), 6.94-6.91 (0.5H, m), 6.88-6.85 (0.5H, m), 6.70 (0.5H, s), 6.65 (0.5H, s), 4.48-4.43 (1H, m), 4.28-4.08 (3.5H, m), 4.06-4.00 (0.5H, m), 3.93-3.80 (2H, m), 3.76-3.68 (2H, m), 2.70-2.61 (2H, m), 2.55-2.41 (2H, m), 2.21-2.07 (1H, m), 1.96-1.75 (3H, m), 1.64-1.52 (2H, m), 1.42-1.23 (9H, m), 0.91-0.85 (3H, m).

Example 135

Ethyl (2R,3R)-8-[N-(2-heptylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-910)



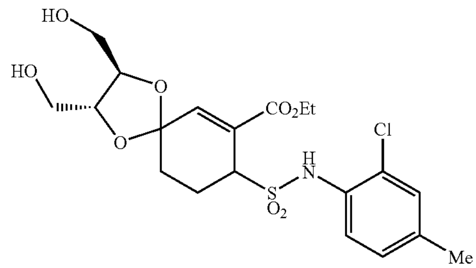
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2-heptylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 5 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as a colorless oil (yield: 33%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.54-7.50 (1H, m), 7.23-7.18 (2H, m), 7.14-7.09 (1H, m), 6.94-6.91 (0.5H, m), 6.88-6.85 (0.5H, m), 6.70 (0.5H, s), 6.65 (0.5H, s), 4.47-4.43 (1H, m), 4.28-4.08 (3.5H, m), 4.06-4.00 (0.5H, m), 3.93-3.80 (2H, m), 3.76-3.68 (2H, m), 2.70-2.61 (2H, m), 2.54-2.41 (2H, m), 2.20-2.08 (1H, m), 1.96-1.74 (3H, m), 1.64-1.53 (2H, m), 1.41-1.22 (11H, m), 0.88 (3H, t, J=7 Hz).

Example 136

Ethyl (2R,3R)-8-[N-(2-chloro-4-methylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-470)



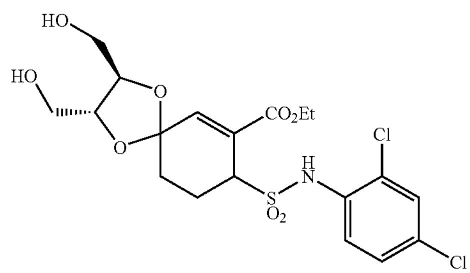
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2-chloro-4-methylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 108 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 50%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.56 (1H, dd, J=8 Hz, 2 Hz), 7.23-7.21 (1H, m), 7.11-7.07 (1H, m), 7.01 (1H, brs), 6.90 (0.5H, t, J=1 Hz), 6.84-6.82 (0.5H, m), 4.44 (1H, dd, J=6 Hz, 2 Hz), 4.27-4.08 (3.5H, m), 4.05-4.00 (0.5H, m), 3.93-3.80 (2H, m), 3.77-3.68 (2H, m), 2.63-2.44 (2H, m), 2.31 (3H, s), 2.22-1.62 (4H, m), 1.29-1.23 (3H, m).

Example 137

Ethyl (2R,3R)-8-[N-(2,4-dichlorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2499)



Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2,4-dichlorophenyl) sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 106 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 22%).

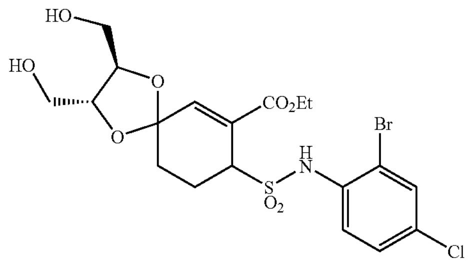
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.64 (1H, dd, J=9 Hz, 2 Hz), 7.41 (1H, d, J=2 Hz), 7.28-7.25 (1H, m), 7.07 (1H, brs), 6.91 (0.5H, t, J=1 Hz), 6.85 (0.5H, t, J=1 Hz), 4.43 (1H, dd, J=6 Hz, 2 Hz), 4.26-4.09

(3.5H, m), 4.07-4.02 (0.5H, m), 3.94-3.81 (2H, m), 3.77-3.68 (2H, m), 2.60-2.47 (2H, m), 2.24-1.85 (4H, m), 1.29-1.24 (3H, m).

Example 138

Ethyl (2R,3R)-8-[N-(2-bromo-4-chlorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2408)



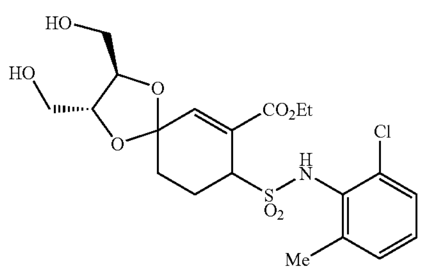
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2-bromo-4-chlorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 93 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 10%).

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.64 (1H, dd, J=9 Hz, 3 Hz), 7.57 (1H, d, J=2 Hz), 7.31 (1H, dd, J=9 Hz, 2 Hz), 7.01 (1H, brs), 6.91 (0.5H, s), 6.85 (0.5H, s), 4.45 (1H, d, J=4 Hz), 4.26-4.10 (3.5H, m), 4.06-4.02 (0.5H, m), 3.94-3.82 (2H, m), 3.77-3.69 (2H, m), 2.61-2.48 (2H, m), 2.24-2.15 (1H, m), 2.02-1.85 (3H, m), 1.29-1.24 (3H, m).

Example 139

Ethyl (2R,3R)-8-[N-(2-chloro-6-methylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1480)



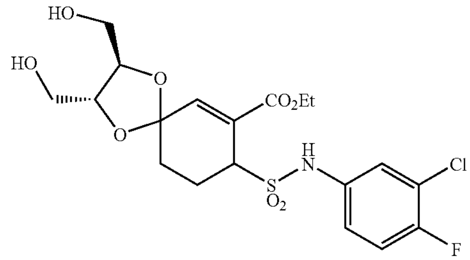
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2-chloro-6-methylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 112 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 45%).

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.28 (1H, dd, J=8 Hz, 1 Hz), 7.23-7.07 (3H, m), 6.93-6.91 (0.5H, m), 6.86-6.85 (0.5H, m), 4.80-4.76 (1H, m), 4.30-4.17 (3H, m), 4.11-4.07 (0.5H, m), 4.04-4.00 (0.5H, m), 3.92-3.81 (2H, m), 3.75-3.69 (2H, m), 2.59-2.48 (3H, m), 2.42-2.33 (1H, m), 2.26-2.15 (1H, m), 2.07 (1H, brs), 1.94-1.85 (1H, m), 1.63 (1H, brs), 1.29-1.24 (3H, m).

Example 140

Ethyl (2R,3R)-8-[N-(3-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2366)



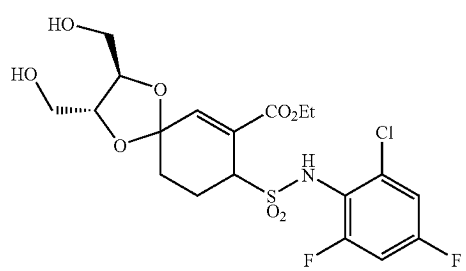
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(3-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 80 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 47%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.47 (1H, dd, J=6 Hz, 3 Hz), 7.29-7.25 (1H, m), 7.17-7.06 (2H, m), 6.97 (0.5H, t, J=1 Hz), 6.93-6.92 (0.5H, m), 4.33-4.09 (4.5H, m), 4.06-4.02 (0.5H, m), 3.94-3.82 (2H, m), 3.77-3.68 (2H, m), 2.48-2.40 (1H, m), 2.34-2.24 (1H, m), 2.12-2.01 (2H, m), 1.97-1.89 (2H, m), 1.35 (3H, t, J=7 Hz).

Example 141

Ethyl (2R,3R)-8-[N-(2-chloro-4,6-difluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2548)



Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2-chloro-4,6-difluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 115 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 35%).

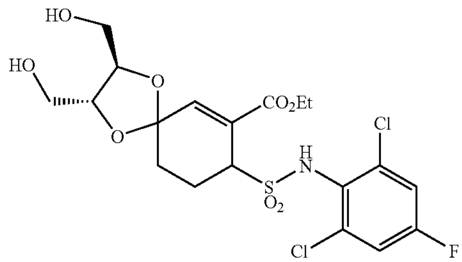
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.07-6.85 (4H, m), 4.67 (1H, dd, J=10 Hz, 6 Hz), 4.32-4.19 (3H, m), 4.14-4.02 (1H, m), 3.93-3.82 (2H, m), 3.76-3.70

(2H, m), 2.66-2.55 (1H, m), 2.43-2.34 (1H, m), 2.28-2.17 (1H, m), 2.06-1.88 (3H, m), 1.33-1.29 (3H, m).

Example 142

Ethyl (2R,3R)-8-[N-(2,6-dichloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2555)



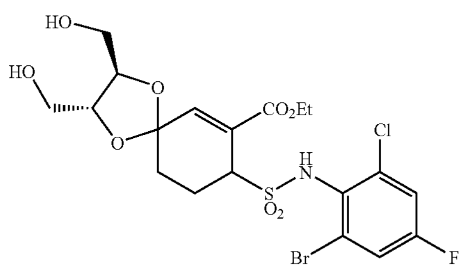
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2,6-dichloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 116 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 25%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.26-7.05 (3H, m), 6.97-6.95 (0.5H, m), 6.90-6.89 (0.5H, m), 4.85-4.80 (1H, m), 4.33-4.19 (3H, m), 4.13-4.08 (0.5H, m), 4.06-4.02 (0.5H, m), 3.93-3.82 (2H, m), 3.76-3.70 (2H, m), 2.72-2.56 (1H, m), 2.39-2.20 (2H, m), 2.05-1.59 (3H, m), 1.35-1.30 (3H, m).

Example 143

Ethyl (2R,3R)-8-[N-(2-bromo-6-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2562)



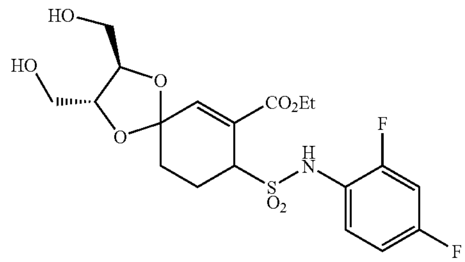
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2-bromo-6-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 117 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 29%).

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.36-7.31 (1H, m), 7.23-7.19 (1H, m), 7.16 (1H, brs), 6.95 (0.5H, s), 6.90-6.88 (0.5H, m), 4.91-4.85 (1H, m), 4.33-4.17 (3H, m), 4.15-4.00 (1H, m), 3.94-3.80 (2H, m), 3.76-3.70 (2H, m), 3.55 (1H, brs), 2.70-2.57 (1H, m), 2.38-2.16 (2H, m), 1.96-1.87 (2H, m), 1.35-1.30 (3H, m).

Example 144

Ethyl (2R,3R)-8-[N-(2,4-difluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-294)



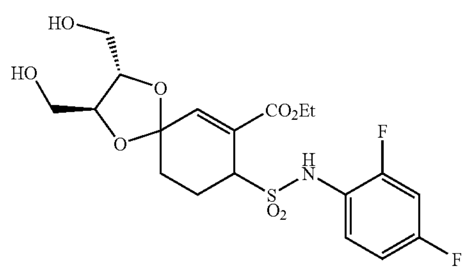
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2,4-difluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 77 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 35%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.63-7.56 (1H, m), 7.07 (1H, brs), 6.94-6.85 (3H, m), 4.38-4.34 (1H, m), 4.30-4.08 (3.5H, m), 4.06-4.00 (0.5H, m), 3.93-3.81 (2H, m), 3.78-3.68 (2H, m), 2.53-2.40 (2H, m), 2.38-1.87 (4H, m), 1.31-1.27 (3H, m).

Example 145

Ethyl (2S,3S)-8-[N-(2,4-difluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-294)



Following the process described in Examples 7, (16a) and 18 (alternative procedure), ethyl 8-[N-(2,4-difluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 77 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 58%).

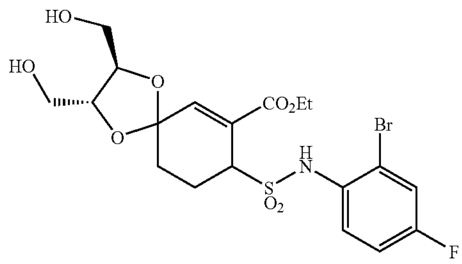
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.62-7.57 (1H, m), 6.93-6.86 (3H, m), 4.37-4.34 (1H, m), 4.29-4.18 (3H, m), 4.13-4.09 (0.5H, m), 4.06-4.01 (0.5H, m),

3.94-3.82 (2H, m), 3.76-3.69 (2H, m), 2.53-2.39 (2H, m), 2.21-1.50 (4H, m), 1.32-1.27 (3H, m).

Example 146

Ethyl (2R,3R)-8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1568)



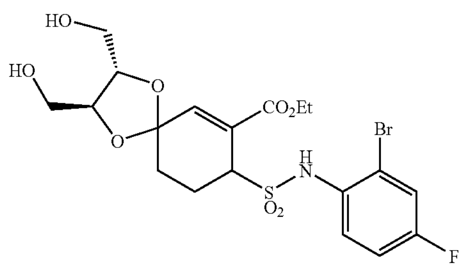
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 78 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 33%).

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.69-7.64 (1H, m), 7.33 (1H, dd, J=7 Hz, 3 Hz), 7.10-7.05 (1H, m), 6.93 (1H, brs), 6.93 (0.5H, s), 6.84 (0.5H, s), 4.44 (1H, d, J=4 Hz), 4.27-4.09 (3.5H, m), 4.06-4.01 (0.5H, m), 3.94-3.80 (2H, m), 3.77-3.68 (2H, m), 3.54 (1H, brs), 2.61-2.46 (2H, m), 2.23-2.14 (1H, m), 2.02-1.85 (2H, m), 1.29-1.24 (3H, m).

Example 147

Ethyl (2S,3S)-8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1568)



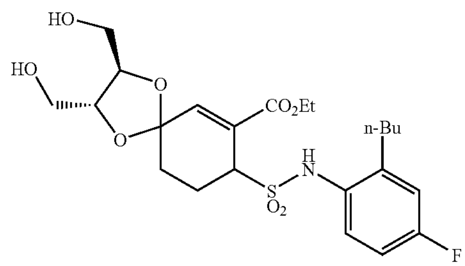
Following the process described in Examples 7, (16a) and 18 (alternative procedure), ethyl 8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 78 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as a white amorphous substance (yield: 49%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.69-7.65 (1H, m), 7.33 (1H, dd, J=8 Hz, 3 Hz), 7.10-7.06 (1H, m), 6.99 (1H, brs), 6.91 (0.5H, s), 6.83 (0.5H, s), 4.44 (1H, d, J=4 Hz), 4.24-3.73 (8H, m), 2.61-2.48 (2H, m), 2.61-2.48 (1H, m), 1.96-1.87 (1H, m), 1.26 (3H, t, J=6 Hz).

Example 148

Ethyl (2R,3R)-8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-646)



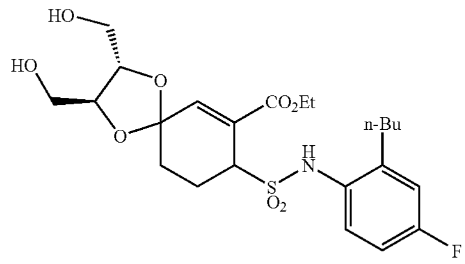
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 85 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as a pale red amorphous substance (yield: 40%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.51-7.45 (1H, m), 6.97-6.85 (3H, m), 6.65 (0.5H, s), 6.59 (0.5H, s), 4.43-4.36 (1H, m), 4.29-4.16 (3H, m), 4.13-4.08 (0.5H, m), 4.07-4.01 (0.5H, m), 3.95-3.80 (2H, m), 3.77-3.68 (2H, m), 2.78-2.62 (2H, m), 2.53-2.35 (2H, m), 2.19-1.84 (4H, m), 1.65-1.49 (2H, m), 1.44-1.35 (2H, m), 1.33-1.27 (3H, m), 0.95 (3H, t, J=7 Hz).

Example 149

Ethyl (2S,3S)-8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-646)



Following the process described in Examples 7, (16a) and 18 (alternative procedure), ethyl 8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 85 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as a pale red amorphous substance (yield: 14%).

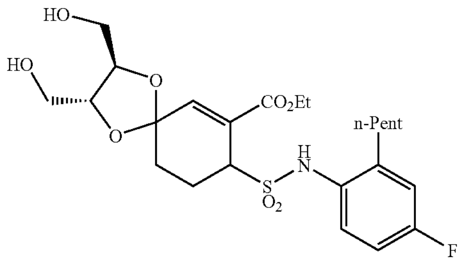
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.50-7.44 (1H, m), 6.98-6.86 (3H, m), 6.73 (0.4H, s), 6.68 (0.6H, s), 4.43-4.37 (1H, m), 4.26-4.16 (3H, m), 4.11-4.07 (0.4H, m), 4.05-3.99 (0.6H, m), 3.90-3.80 (2H, m), 3.78-3.68 (2H, m), 2.77-2.62 (2H, m), 2.53-2.23 (3H, m), 2.20-2.07

(2H, m), 1.96-1.86 (1H, m), 1.63-1.53 (2H, m), 1.44-1.34 (2H, m), 1.32-1.26 (3H, m), 0.95 (3H, t, J=7 Hz).

Example 150

Ethyl (2R,3R)-8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1744)



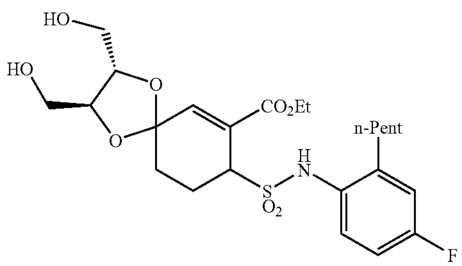
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 86 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as a pale red amorphous substance (yield: 33%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.50-7.43 (1H, m), 6.97-6.85 (3H, m), 6.67 (0.5H, s), 6.61 (0.5H, s), 4.42-4.37 (1H, m), 4.30-4.17 (3H, m), 4.12-4.08 (0.5H, m), 4.05-4.01 (0.5H, m), 3.93-3.82 (2H, m), 3.76-3.68 (2H, m), 2.77-2.61 (2H, m), 2.53-2.35 (2H, m), 2.19-1.80 (4H, m), 1.66-1.50 (2H, m), 1.40-1.22 (7H, m), 0.95-0.87 (3H, m).

Example 151

Ethyl (2S,3S)-8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1744)



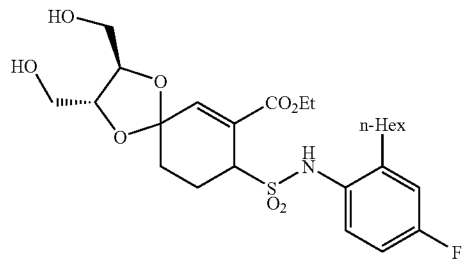
Following the process described in Examples 7, (16a) and 18 (alternative procedure), ethyl 8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 86 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as a pale red amorphous substance (yield: 30%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.50-7.42 (1H, m), 6.97-6.84 (3H, m), 6.77 (0.5H, s), 6.72 (0.5H, s), 4.42-4.36 (1H, m), 4.30-4.14 (3H, m), 4.12-4.05 (0.5H, m), 4.04-3.98 (0.5H, m), 3.91-3.77 (2H, m), 3.76-3.67 (2H, m), 2.76-2.59 (2H, m), 2.53-2.20 (4H, m), 2.20-2.06 (1H, m), 1.97-1.84 (1H, m), 1.66-1.52 (2H, m), 1.41-1.22 (7H, m), 0.95-0.88 (3H, m).

Example 152

Ethyl (2R,3R)-8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-822)



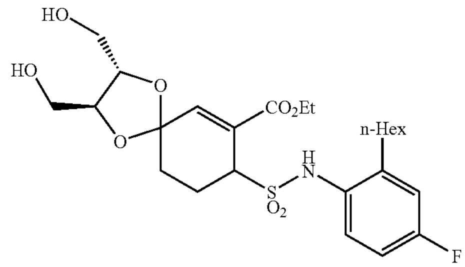
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 87 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 54%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.50-7.45 (1H, m), 6.96-6.86 (3H, m), 6.67 (0.5H, s), 6.61 (0.5H, s), 4.41-4.37 (1H, m), 4.30-4.16 (3H, m), 4.13-4.08 (0.5H, m), 4.06-4.01 (0.5H, m), 3.93-3.81 (2H, m), 3.76-3.69 (2H, m), 2.76-2.61 (2H, m), 2.52-2.36 (2H, m), 2.20-1.50 (6H, m), 1.41-1.26 (9H, m), 0.91-0.85 (3H, m).

Example 153

Ethyl (2S,3S)-8-E[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-822)



Following the process described in Examples 7, (16a) and 18 (alternative procedure), ethyl 8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 87 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 54%).

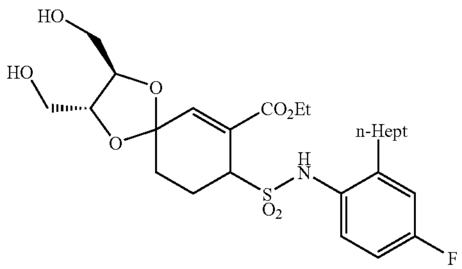
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.50-7.44 (1H, m), 6.96-6.86 (3H, m), 6.70-6.67 (0.5H, m), 6.64-6.61 (0.5H, m), 4.41-4.37 (1H, m), 4.29-4.15 (3H, m), 4.12-4.07 (0.5H, m), 4.05-4.00 (0.5H, m), 3.93-3.80 (2H, m),

3.76-3.68 (2H, m), 2.76-2.61 (2H, m), 2.52-2.35 (2H, m), 2.31-1.51 (6H, m), 1.40-1.26 (9H, m), 0.91-0.86 (3H, m).

Example 154

Ethyl (2R,3R)-8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-998)



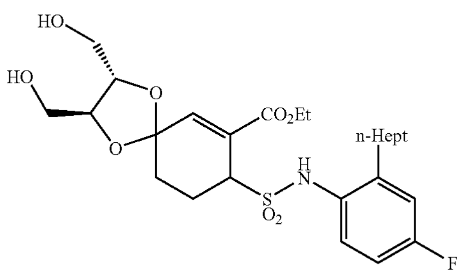
Following the process described in Example 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 88 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 41%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, m), 6.96-6.87 (3H, m), 6.68 (0.5H, s), 6.61 (0.5H, s), 4.41-4.40 (1H, m), 4.30-3.71 (8H, m), 2.72-2.65 (2H, m), 2.48-2.39 (2H, m), 2.14-2.10 (2H, m), 1.95-1.87 (2H, m), 1.37-1.22 (11H, m), 0.88 (3H, t, J=7 Hz).

Example 155

Ethyl (2S,3S)-8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-998)



Following the process described in Examples 7, (16a) and 18 (alternative procedure), ethyl 8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 88 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as a white amorphous substance (yield: 70%).

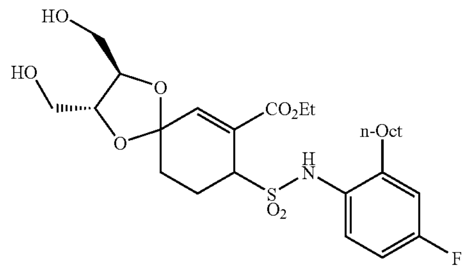
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.50, 7.48 (1H, m), 6.97-6.88 (3H, m), 6.70 (0.5H, s), 6.70 (0.5H, s), 4.41-4.39 (1H, m), 4.28-3.71 (8H, m), 2.75-2.63

(2H, m), 2.51-2.37 (2H, m), 2.19-2.10 (2H, m), 1.95-1.88 (2H, m), 1.35-1.23 (11H, m), 0.88 (3H, t, J=7 Hz).

Example 156

Ethyl (2R,3R)-8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1920)



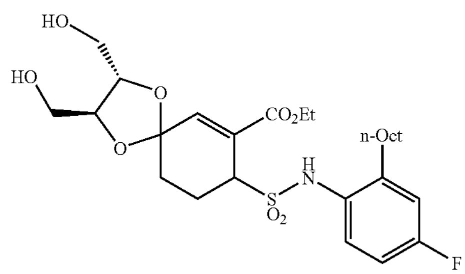
Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 89 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 47%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.51-7.47 (1H, m), 6.97-6.88 (3H, m), 6.71 (0.5H, s), 6.64 (0.5H, s), 4.41-4.39 (1H, m), 4.28-3.72 (8H, m), 2.76-2.62 (2H, m), 2.51-2.37 (2H, m), 2.18-1.89 (4H, m), 1.37-1.27 (13H, m), 0.88 (3H, t, J=7 Hz).

Example 157

Ethyl (2S,3S)-8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-1920)



Following the process described in Examples 7, (16a) and 18 (alternative procedure), ethyl 8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 89 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 51%).

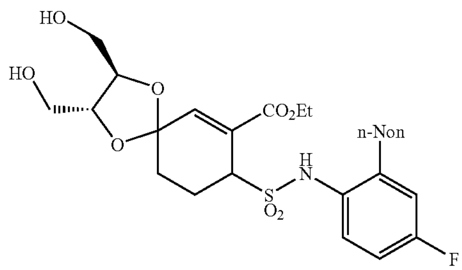
^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, dd, J=9 Hz, 5 Hz), 6.97-6.88 (3H, m), 6.69 (0.5H, s), 6.63 (0.5H, s), 4.41-4.39 (1H, m), 4.31-3.70 (8H, m),

2.72-2.66 (2H, m), 2.52-2.37 (2H, m), 2.19-1.88 (4H, m), 1.37-1.27 (13H, m), 0.88 (3H, t, J=7 Hz).

Example 158

Ethyl (2R,3R)-8-[1N-(4-fluoro-2-nonylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2604)



Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(4-fluoro-2-nonylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 90 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 48%). This compound was separable into two optical isomers in accordance with the following HPLC conditions.

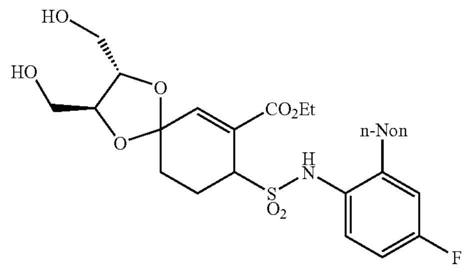
HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 7:3
Fow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 4.43 minutes high polarity compound (second peak): 4.73 minutes

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.50-7.45 (1H, m), 6.97-6.86 (3H, m), 6.66 (0.5H, s), 6.60 (0.5H, s), 4.42-4.37 (1H, m), 4.28-4.18 (3H, m), 4.13-4.08 (0.5H, m), 4.06-4.01 (0.5H, m), 3.95-3.81 (2H, m), 3.76-3.69 (2H, m), 2.77-2.61 (2H, m), 2.53-2.35 (2H, m), 2.19-1.99 (2H, m), 1.96-1.86 (2H, m), 1.64-1.52 (2H, m), 1.40-1.18 (15H, m), 0.91-0.85 (3H, m).

Example 159

Ethyl (2S,3S)-8-[N-(4-fluoro-2-nonylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2604)



Following the process described in Examples 7, (16a) and 18 (alternative procedure), ethyl 8-[N-(4-fluoro-2-nonylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 90 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 54%). This compound was separable into two optical isomers in accordance with the following HPLC conditions.

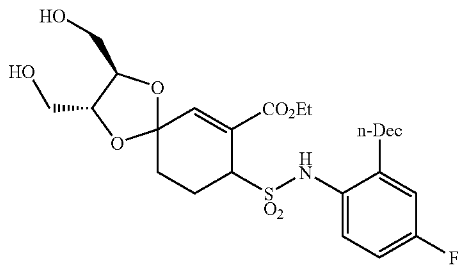
HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 4:1
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 6.7 minutes high polarity compound (second peak): 10.1 minutes

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.50-7.45 (1H, m), 6.97-6.86 (3H, m), 6.71 (0.5H, s), 6.65 (0.5H, s), 4.42-4.37 (1H, m), 4.30-4.16 (3H, m), 4.13-4.08 (0.5H, m), 4.05-4.00 (0.5H, m), 3.93-3.80 (2H, m), 3.77-3.69 (2H, m), 2.76-2.61 (2H, m), 2.52-2.01 (5H, m), 1.95-1.86 (1H, m), 1.64-1.52 (2H, m), 1.41-1.22 (15H, m), 0.88 (3H, t, J=7 Hz).

Example 160

Ethyl (2R,3R)-8-[N-(2-decyl-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2618)



Following the process described in Examples 7, (16a) and 17 (alternative procedure), ethyl 8-[N-(2-decyl-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 91 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 35%). This compound was separable into two optical isomers in accordance with the following HPLC conditions.

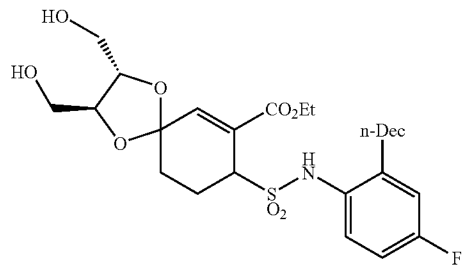
HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 7:3
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 4.30 minutes high polarity compound (second peak): 4.55 minutes

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.51-7.45 (1H, m), 6.97-6.86 (3H, m), 6.67 (0.5H, s), 6.61 (0.5H, s), 4.42-4.36 (1H, m), 4.30-4.17 (3H, m), 4.13-4.08 (0.5H, m), 4.06-4.01 (0.5H, m), 3.94-3.80 (2H, m), 3.76-3.69 (2H, m), 2.76-2.61 (2H, m), 2.53-2.35 (2H, m), 2.19-2.00 (2H, m), 1.99-1.86 (2H, m), 1.65-1.51 (2H, m), 1.40-1.18 (17H, m), 0.91-0.85 (3H, m).

Example 161

Ethyl (2S,3S)-8-[N-(2-decyl-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2618)



Following the process described in Examples 7, (16a) and 18 (alternative procedure), ethyl 8-[N-(2-decyl-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 91 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 56%). This compound was separable into two optical isomers in accordance with the following HPLC conditions.

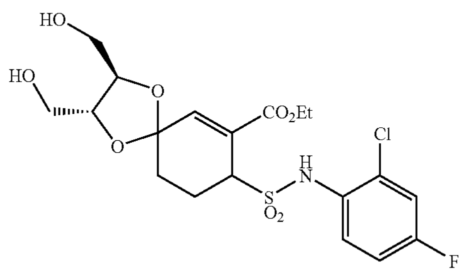
HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 4:1
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 6.4 minutes high polarity compound (second peak): 9.1 minutes

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.50-7.45 (1H, m), 6.97-6.87 (3H, m), 6.70 (0.5H, s), 6.64 (0.5H, s), 4.42-4.38 (1H, m), 4.30-4.17 (3H, m), 4.12-4.08 (0.5H, m), 4.05-4.01 (0.5H, m), 3.93-3.81 (2H, m), 3.78-3.69 (2H, m), 2.76-2.62 (2H, m), 2.52-2.37 (2H, m), 2.33-2.09 (2H, m), 2.06-1.87 (2H, m), 1.63-1.52 (2H, m), 1.40-1.22 (17H, m), 0.88 (3H, t, J=7 Hz).

Example 162

Ethyl (2R,3R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-382)



Ethyl (2R,3R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 17 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as a white amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 4:1
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 12.0 minutes high polarity compound (second peak): 16.5 minutes

(Low Polarity Compound, First Peak)

Optical rotation $[\alpha]_D$+86.7 (c=2.0, MeOH)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.67 (1H, dd, J=9 Hz, 5 Hz), 7.17 (1H, dd, J=8 Hz, 3 Hz), 7.07-6.98 (2H, m), 6.91 (1H, s), 4.42 (1H, dd, J=6 Hz, 2 Hz), 4.28-4.08 (4H, m), 3.91 (1H, dd, J=12 Hz, 4 Hz), 3.84 (1H, dd, J=12 Hz, 4 HZ), 3.77-3.68 (2H, m), 2.60-2.43 (2H, m), 2.26-2.11 (1H, m), 1.99-1.87 (1H, m), 1.58 (2H, bs), 1.27 (3H, t, J=7 Hz).

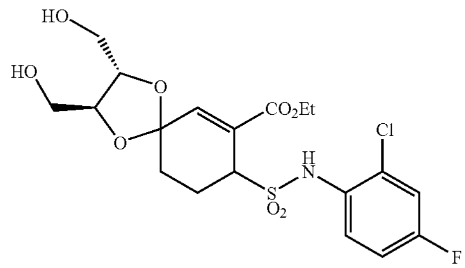
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.66 (1H, dd, J=9 Hz, 5 Hz), 7.17 (1H, dd, J=8 Hz, 3 Hz), 7.07-6.98 (2H, m), 6.84 (1H, s), 4.42 (1H, d, J=5 Hz), 4.28-4.08 (3H, m), 4.07-4.01 (1H, m), 3.93-3.82 (2H, m), 3.77-3.68 (2H, m), 2.61-2.46 (2H, m), 2.24-2.11 (1H, m), 1.95-1.87 (1H, m), 1.57 (2H, bs), 1.27 (3H, t, J=7 Hz).

Example 163

Ethyl (2S,3S)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-382)



Ethyl (2S,3S)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 18 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as a white amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 4:1
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 11.4 minutes high polarity compound (second peak): 27.4 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.66 (1H, dd, J=9 Hz, 5 Hz), 7.17 (1H, dd, J=8 Hz, 3 Hz), 7.06-7.00 (1H, m), 6.98 (1H, s), 6.84 (1H, s), 4.42 (1H, d, J=5 Hz), 4.27-4.09 (3H, m), 4.07-4.00 (1H, m), 3.93-3.83 (2H, m), 3.76-3.68 (2H, m), 2.60-2.47 (2H, m), 2.24-2.12 (1H, m), 1.95-1.60 (3H, m), 1.27 (3H, t, J=7 Hz).

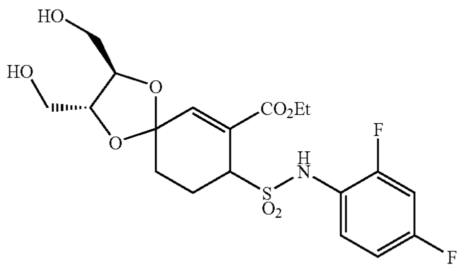
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.67 (1H, dd, J=9 Hz, 5 Hz), 7.17 (1H, dd, J=8 Hz, 3 Hz), 7.06-6.99 (2H, m), 6.90 (1H, s), 4.44-4.41 (1H, m), 4.27-4.09 (4H, m), 3.91 (1H, dd, J=12 Hz, 4 Hz), 3.84 (1H, dd, J=12 Hz, 4 HZ), 3.77-3.68 (2H, m), 2.60-2.45 (2H, m), 2.24-2.12 (1H, m), 2.00-1.65 (3H, m), 1.27 (3H, t, J=7 Hz).

Example 164

Ethyl (2R,3R)-8-[N-(2,4-difluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-294)



Ethyl (2R,3R)-8-[N-(2,4-difluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 144 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as an amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 4:1
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 13.7 minutes high polarity compound (second peak): 15.9 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.62-7.57 (1H, m), 6.93-6.87 (3H, m), 4.36 (1H, q, J=3 Hz), 4.28-4.18 (3H, m), 4.15-4.09 (1H, m), 3.91 (1H, dd, J=12 Hz, 4 Hz), 3.84 (1H, dd, J=12 Hz, 4 Hz), 3.75-3.70 (2H, m), 2.51-2.40 (2H, m), 2.20-2.12 (1H, m), 1.96-1.90 (1H, m), 1.61 (2H, brs), 1.29 (3H, t, J=7 Hz).

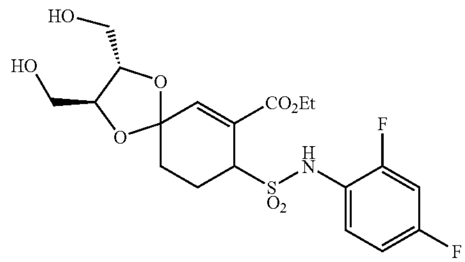
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.62-7.57 (1H, m), 6.97 (1H, brs), 6.93-6.86 (3H, m), 4.37-4.35 (1H, m), 4.29-4.17 (3H, m), 4.06-4.02 (1H, m), 3.91-3.84 (2H, m), 3.76-3.69 (2H, m), 2.53-2.41 (2H, m), 2.20-2.11 (1H, m), 2.05 (1H, brs), 1.94-1.88 (2H, m), 1.29 (3H, t, J=7 Hz).

Example 165

Ethyl (2S,3S)-8-[N-(2,4-difluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-294)



Ethyl (2S,3S)-8-[N-(2,4-difluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 145 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as an amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 7:3
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 6.9 minutes high polarity compound (second peak): 10.7 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.62-7.57 (1H, m), 6.93-6.86 (3H, m), 4.36 (1H, d, J=4 Hz), 4.29-4.18 (3H, m), 4.06-4.01 (1H, m), 3.91-3.84 (2H, m), 3.75-3.70 (2H, m), 2.52-2.42 (2H, m), 2.19-1.50 (4H, m), 1.29 (3H, t, J=7 Hz).

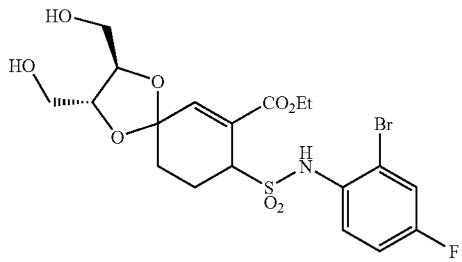
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.62-7.57 (1H, m), 6.93-6.87 (3H, m), 4.36 (1H, dd, J=6 Hz, 3 Hz), 4.29-4.18 (3H, m), 4.13-4.09 (1H, m), 3.91 (1H, dd, J=12 Hz, 4 Hz), 3.84 (1H, dd, J=12 Hz, 4 Hz), 3.75-3.70 (2H, m), 2.51-2.40 (2H, m), 2.20-1.50 (4H, m), 1.29 (3H, t, J=7 Hz).

Example 166

Ethyl (2R,3R)-8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-1568)



Ethyl (2R,3R)-8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 146 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as an amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 7:3
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 6.8 minutes high polarity compound (second peak): 8.8 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.68 (1H, dd, J=9.2 Hz, 5.2 Hz), 7.34 (1H, dd, J=7.6 Hz, 2.9 Hz), 7.11-7.06 (1H, m), 6.91 (1H, s), 4.44 (1H, dd, J=5.8 Hz, 2.0 Hz), 4.28-4.10 (4H, m), 3.93-3.70 (4H, m), 2.60-2.47 (2H, m), 2.24-2.14 (1H, m), 1.97-1.92 (1H, m), 1.27 (3H, t, J=7.0 Hz).

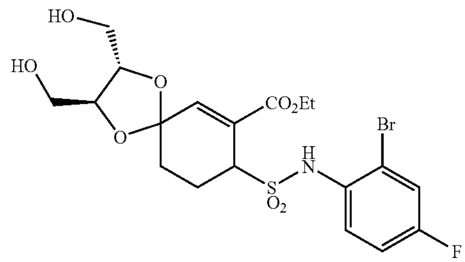
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.67 (1H, dd, J=9.2 Hz, 5.3 Hz), 7.34 (1H, dd, J=7.6 Hz, 2.9 Hz), 7.11-7.06 (1H, m), 6.85 (1H, s), 4.44 (1H, d, J=5.0 Hz), 4.27-4.02 (4H, m), 3.92-3.84 (2H, m), 3.76-3.70 (2H, m), 2.61-2.48 (2H, m), 2.23-2.15 (1H, m), 1.92-1.88 (1H, m), 1.27 (3H, t, J=7.2 Hz).

Example 167

Ethyl (2S,3S)-8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-1568)



Ethyl (2S,3S)-8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 147 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as an amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 7:3
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 6.7 minutes high polarity compound (second peak): 13.2 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.67 (1H, dd, J=9 Hz, 5 Hz), 7.33 (1H, dd, J=8 Hz, 3 Hz), 7.10-7.06 (1H, m), 6.84 (1H, s), 4.44 (1H, d, J=5 Hz), 4.24-3.70 (8H, m), 2.61-2.48 (2H, m), 2.24-1.87 (2H, m), 1.26 (3H, t, J=7 Hz).

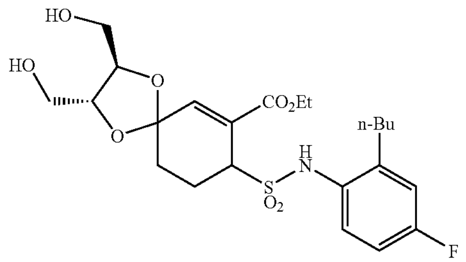
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.67 (1H, dd, J=9 Hz, 5 Hz), 7.33 (1H, dd, J=8 Hz, 3 Hz), 7.10-7.05 (1H, m), 6.91 (1H, s), 4.44 (1H, d, J=6 Hz), 4.27-3.69 (8H, m), 2.59-2.48 (2H, m), 2.23-1.91 (2H, m), 1.26 (3H, t, J=7 Hz).

Example 168

Ethyl (2R,3R)-8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-646)



Ethyl (2R,3R)-8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 148 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as a pale red amorphous substance and a white powder. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 7:3
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 5.02 minutes high polarity compound (second peak): 5.24 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, dd, J=9 Hz, 5 Hz), 6.98-6.93 (2H, m), 6.90 (1H, dt, J=8 Hz, 3 Hz), 6.67 (1H, s), 4.40 (1H, dd, J=6 Hz, 3 Hz), 4.29-4.19 (3H, m), 4.13-4.08 (1H, m), 3.92 (1H, dd, J=12 Hz, 4 Hz), 3.85 (1H, dd, 12 Hz, 4 Hz), 3.76-3.69 (2H, m), 2.78-2.62 (2H, m), 2.53-2.35 (2H, m), 2.19-1.80 (4H, m), 1.65-1.49 (2H, m), 1.44-1.34 (2H, m), 1.31 (3H, t, J=7 Hz), 0.95 (3H, t, J=7 Hz).

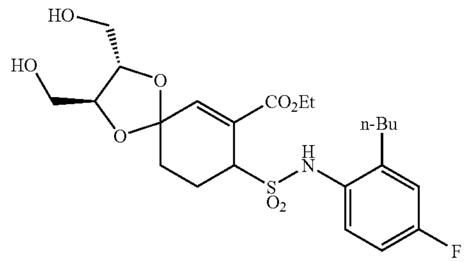
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.48 (1H, dd, J=9 Hz, 5 Hz), 6.95 (1H, dd, J=9 Hz, 3 Hz), 6.93-6.86 (2H, m), 6.62 (1H, s), 4.41 (1H, d, J=4 Hz), 4.28-4.17 (3H, m), 4.05-4.01 (1H, m), 3.91-3.83 (2H, m), 3.77-3.69 (2H, m), 2.77-2.62 (2H, m), 2.53-2.35 (2H, m), 2.18-1.76 (4H, m), 1.65-1.50 (2H, m), 1.44-1.35 (2H, m), 1.30 (3H, t, J=7 Hz), 0.95 (3H, t, J=7 Hz).

Example 169

Ethyl (2S,3S)-8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-646)



Ethyl (2S,3S)-8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 149 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as a white powder and a pale red amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 7:3
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 5.08 minutes high polarity compound (second peak): 5.58 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.47 (1H, dd, J=9 Hz, 5 Hz), 6.95 (1H, dd, J=9 Hz, 3 Hz), 6.93-6.86 (2H, m), 6.61 (1H, s), 4.41 (1H, d, J=4 Hz), 4.26-4.16 (3H, m), 4.05-3.99 (1H, m), 3.90-3.80 (2H, m), 3.78-3.68 (2H, m), 2.77-2.62 (2H, m), 2.53-2.39 (2H, m), 2.33-2.05 (2H, m), 1.96-1.86 (1H, m), 1.80-1.65 (1H, m), 1.63-1.52 (2H, m), 1.44-1.35 (2H, m), 1.29 (3H, t, J=7 Hz), 0.95 (3H, t, J=7 Hz).

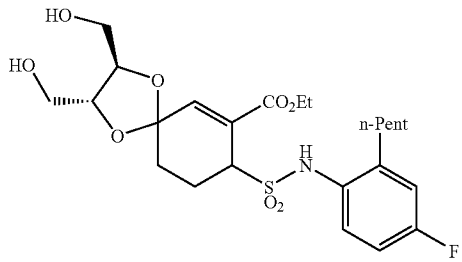
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.48 (1H, dd, J=9 Hz, 5 Hz), 6.99-6.86 (3H, m), 6.70 (1H, s), 4.40 (1H, dd, J=6 Hz, 3 Hz), 4.29-4.17 (3H, m), 4.13-4.07 (1H, m), 3.90 (1H, dd, J=12 Hz, 4 Hz), 3.84 (1H, dd, 12 Hz, 4 Hz), 3.76-3.69 (2H, m), 2.77-2.62 (2H, m), 2.53-2.23 (3H, m), 2.20-2.00 (2H, m), 1.96-1.86 (1H, m), 1.63-1.52 (2H, m), 1.44-1.34 (2H, m), 1.30 (3H, t, J=7 Hz), 0.95 (3H, t, J=7 Hz).

Example 170

Ethyl (2R,3R)-8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-1744)



Ethyl (2R,3R)-8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 150 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as a pale red amorphous substance and a white powder. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 7:3
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 4.83 minutes high polarity compound (second peak): 5.01 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.48 (1H, dd, J=9 Hz, 5 Hz), 6.97-6.92 (2H, m), 6.90 (1H, dt, J=8 Hz, 3 Hz), 6.66 (1H, s), 4.40 (1H, dd, J=6 Hz, 3 Hz), 4.28-4.18 (3H, m), 4.14-4.07 (1H, m), 3.92 (1H, dd, J=12 Hz, 4 Hz), 3.85 (1H, dd, 12 Hz, 4 Hz), 3.76-3.69 (2H, m), 2.76-2.61 (2H, m), 2.50-2.35 (2H, m), 2.19-2.08 (1H, m), 1.97-1.87 (1H, m), 1.81-1.49 (4H, m), 1.40-1.32 (4H, m), 1.30 (3H, t, J=7 Hz), 0.90 (3H, t, J=7 Hz).

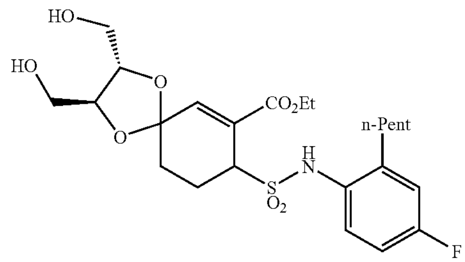
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.48 (1H, dd, J=9 Hz, 5 Hz), 6.95 (1H, dd, J=9 Hz, 3 Hz), 6.93-6.86 (2H, m), 6.60 (1H, s), 4.41 (1H, d, J=5 Hz), 4.29-4.17 (3H, m), 4.07-4.01 (1H, m), 3.93-3.84 (2H, m), 3.76-3.69 (2H, m), 2.76-2.61 (2H, m), 2.54-2.36 (2H, m), 2.19-2.07 (1H, m), 2.06-1.70 (3H, m), 1.66-1.50 (2H, m), 1.40-1.32 (4H, m), 1.30 (3H, t, J=7 Hz), 0.90 (3H, t, J=7 Hz).

Example 171

Ethyl (2S,3S)-8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-1744)



Ethyl (2S,3S)-8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 151 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as a white powder and a pale red amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purity were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 7:3
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 4.90 minutes high polarity compound (second peak): 6.18 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.48 (1H, dd, J=9 Hz, 5 Hz), 6.97-6.85 (3H, m), 6.59 (1H, s), 4.40 (1H, d, J=5 Hz), 4.29-4.17 (3H, m), 4.06-4.00 (1H, m), 3.91-3.83 (2H, m), 3.76-3.69 (2H, m), 2.76-2.59 (2H, m), 2.53-2.36 (2H, m), 2.20-2.06 (1H, m), 1.94-1.85 (1H, m), 1.80-1.50 (4H, m), 1.41-1.22 (7H, m), 0.91 (3H, t, J=7 Hz).

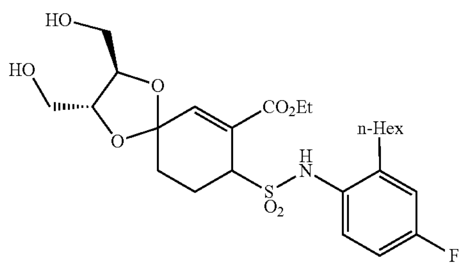
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.47 (1H, dd, J=9 Hz, 5 Hz), 6.97-6.92 (2H, m), 6.89 (1H, dt, J=8 Hz, 3 Hz), 6.73 (1H, s), 4.40 (1H, dd, J=6 Hz, 3 Hz), 4.28-4.17 (3H, m), 4.12-4.05 (1H, m), 3.89 (1H, dd, J=12 Hz, 4 Hz), 3.82 (1H, dd, 12 Hz, 4 Hz), 3.76-3.69 (2H, m), 2.76-2.61 (2H, m), 2.51-2.35 (2H, m), 2.26-2.01 (2H, m), 1.97-1.68 (2H, m), 1.66-1.54 (2H, m), 1.41-1.31 (4H, m), 1.29 (3H, t, J=7 Hz), 0.90 (3H, t, J=7 Hz).

Example 172

Ethyl (2R,3R)-8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-822)



Ethyl (2R,3R)-8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 152 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as an amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 9:1
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 25.2 minutes high polarity compound (second peak): 29.3 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.48 (1H, dd, J=9 Hz, 5 Hz), 6.97-6.87 (3H, m), 6.66 (1H, s), 4.41-4.37 (1H, m), 4.29-4.19 (3H, m), 4.13-4.09 (1H, m), 3.95-3.88 (1H, m), 3.87-3.81 (1H, m), 3.77-3.69 (2H, m), 2.77-2.62 (2H, m), 2.51-2.36 (2H, m), 2.19-2.09 (2H, m), 1.95-1.89 (2H, m), 1.63-1.52 (2H, m), 1.40-1.28 (9H, m), 0.91-0.86 (3H, m).

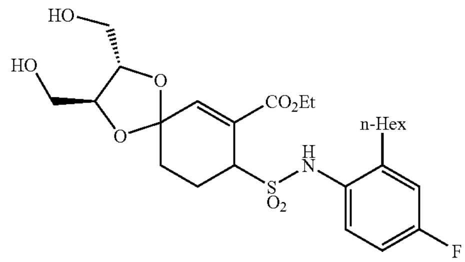
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.47 (1H, dd, J=9 Hz, 5 Hz), 6.96-6.86 (3H, m), 6.63 (1H, s), 4.42-4.39 (1H, m), 4.30-4.16 (3H, m), 4.06-4.01 (1H, m), 3.91-3.83 (2H, m), 3.77-3.69 (2H, m), 2.76-2.61 (2H, m), 2.53-2.37 (2H, m), 2.18-2.08 (2H, m), 2.03-1.98 (1H, m), 1.93-1.86 (1H, m), 1.63-1.52 (2H, m), 1.41-1.26 (9H, m), 0.91-0.86 (3H, m).

Example 173

Ethyl (2S,3S)-8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-822)



Ethyl (2S,3S)-8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 153 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purity two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as an amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 4:1
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 7.6 minutes high polarity compound (second peak): 10.6 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.48 (1H, dd, J=9 Hz, 5 Hz), 6.95 (1H, dd, J=9 Hz, 3 Hz), 6.92-6.87 (2H, m), 6.61 (1H, s), 4.40 (1H, d, J=4 Hz), 4.29-4.17 (3H, m), 4.06-4.02 (1H, m), 3.91-3.84 (2H, m), 3.76-3.70 (2H, m), 2.75-2.62 (2H, m), 2.52-2.46 (1H, m), 2.42 (1H, td, J=14 Hz, 3 Hz), 2.17-2.09 (1H, m), 2.05 (1H, dd, J=8 Hz, 5 Hz), 1.96-1.87 (2H, m), 1.64-1.53 (2H, m), 1.40-1.27 (9H, m), 0.91-0.87 (3H, m).

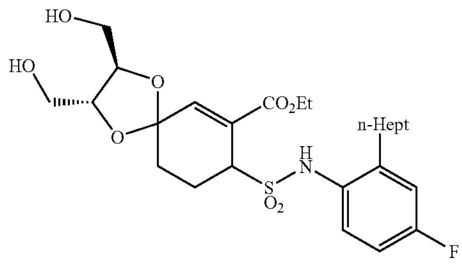
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

7.48 (1H, dd, J=9 Hz, 5 Hz), 6.96-6.93 (2H, m), 6.90 (1H, td, J=8 Hz, 3 Hz), 6.67 (1H, m), 4.39 (1H, dd, J=6 Hz, 4 Hz), 4.30-4.19 (3H, m), 4.13-4.09 (1H, m), 3.91 (1H, dt, J=12 Hz, 4 Hz), 3.84 (1H, dt, J=12 Hz, 4 Hz), 3.76-3.69 (2H, m), 2.76-2.63 (2H, m), 2.50-2.44 (1H, m), 2.40 (1H, td, J=13 Hz, 3 Hz), 2.18-2.10 (2H, m), 1.95-1.89 (2H, m), 1.63-1.53 (2H, m), 1.40-1.28 (9H, m), 0.91-0.87 (3H, m).

Example 174

Ethyl (2R,3R)-8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Low Polarity Compound, First Peak), (High Polarity Compound, Second Peak) (Exemplified Compound No. 1-998)



Ethyl (2R,3R)-8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 154 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify the two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as a white amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 9:1
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 23.9 minutes high polarity compound (second peak): 27.4 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.48 (1H, dd, J=8 Hz, 5 Hz), 6.96-6.88 (3H, m), 6.67 (1H, s), 4.40-4.38 (1H, m), 4.27-3.69 (8H, m), 2.72-2.62 (2H, m), 2.49-1.89 (6H, m), 1.34-1.25 (11H, m), 0.88 (3H, t, J=7 Hz).

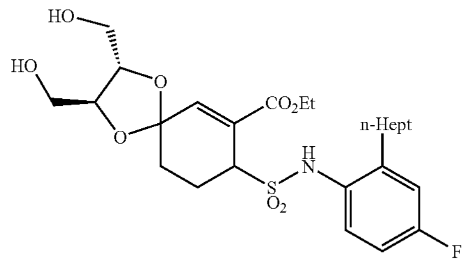
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.47 (1H, dd, J=9 Hz, 5 Hz), 6.96-6.87 (3H, m), 6.64 (1H, brs), 4.40 (1H, d, J=4 Hz), 4.29-3.71 (8H, m), 2.75-2.61 (2H, m), 2.51-2.37 (2H, m), 2.17-1.86 (4H, m), 1.42-1.22 (11H, m), 0.88 (3H, t, J=7 Hz).

Example 175

Ethyl (2S,3S)-8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Low Polarity Compound, First Peak), (High Polarity Compound, Second Peak) (Exemplified Compound No. 1-998)



Ethyl (2S,3S)-8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 155 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as a white powder and a white amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 7:3
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 4.8 minutes high polarity compound (second peak): 6.3 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.48 (1H, dd, J=9 Hz, 5 Hz), 6.97-6.88 (3H, m), 6.64 (1H, s), 4.41 (1H, d, J=4 Hz), 4.27-3.72 (8H, m), 2.75-2.62 (2H, m), 2.51-2.38 (2H, m), 2.18-1.38 (4H, m), 1.38-1.28 (11H, m), 0.88 (3H, t, J=7 Hz).

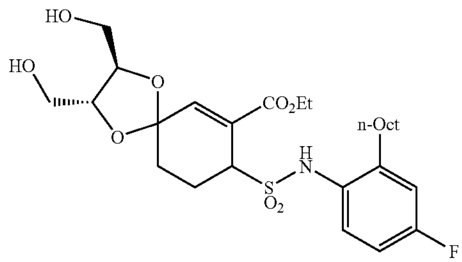
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, dd, J=9 Hz, 5 Hz), 6.97-6.88 (3H, m), 6.69 (1H, s), 4.41-4.39 (1H, m), 4.29-3.71 (8H, m), 2.77-2.62 (2H, m), 2.49-1.90 (6H, m), 1.38-1.29 (11H, m), 0.89 (3H, t, J=7 Hz).

Example 176

Ethyl (2R,3R)-8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Low Polarity Compound, First Peak), (High Polarity Compound, Second Peak) (Exemplified Compound No. 1-1920)



Ethyl (2R,3R)-8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 156 was subjected to high performance liquid chromatography (column; CHIPALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as a white amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 9:1
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 22.9 minutes high polarity compound (second peak): 25.8 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.48 (1H, dd, J=9 Hz, 5 Hz), 6.96-6.88 (3H, m), 6.68 (1H, s), 6.68-4.40 (1H, m), 4.28-3.70 (8H, m), 4.28-3.70 (2H, m), 2.52-1.89 (6H, m), 1.36-1.19 (13H, m), 0.88 (3H, t, J=7 Hz).

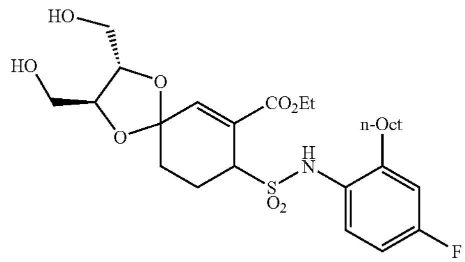
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.46 (1H, dd, J=9 Hz, 5 Hz), 6.95-6.87 (3H, m), 4.40 (1H, d, J=5 Hz), 4.28-3.71 (8H, m), 2.73-2.60 (2H, m), 2.50-1.87 (6H, m), 1.31-1.25 (13H, m), 0.89 (3H, t, J=7 Hz).

Example 177

Ethyl (2S,3S)-8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Low Polarity Compound, First Peak), (High Polarity Compound, Second Peak) (Exemplified Compound No. 1-1920)



Ethyl (2S,3S)-8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 157 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as a white powder and a colorless oil. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 7:3
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 4.7 minutes high polarity compound (second peak): 6.1 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.48 (1H, dd, J=9 Hz, 5 Hz), 6.97-6.88 (3H, m), 6.63 (1H, s), 4.41 (1H, d, J=5 Hz), 4.28-3.71 (8H, m), 2.75-2.62 (2H, m), 2.51-1.88 (6H, m), 1.38-1.27 (13H, m), 0.88 (3H, t, J=7 Hz).

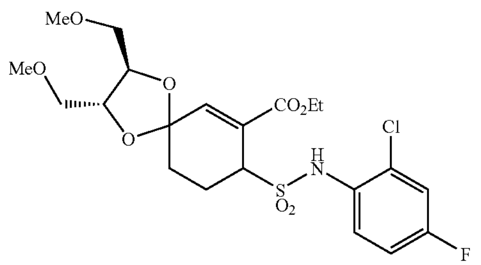
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, dd, J=9 Hz, 6 Hz), 6.97-6.88 (3H, m), 6.97-6.88 (1H, m), 4.41-4.38 (1H, m), 4.31-3.71 (8H, m), 2.77-2.63 (2H, m), 2.50-1.90 (6H, m), 2.50-1.90 (13H, m), 0.88 (3H, t, J=7 Hz).

Example 178

Ethyl (2R,3R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(methoxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate



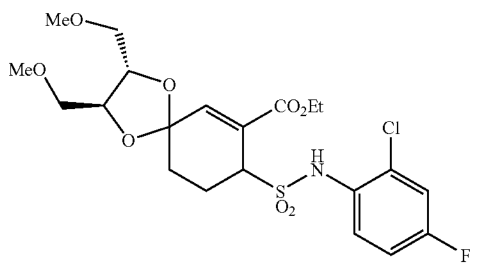
Following the process described in Example (17a), 1,4-di-O-methyl-2,3-di-O-trimethylsilyl-D-threitol was used in place of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-D-threitol to give the title compound as a colorless oil (yield: 89%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.68-7.64 (1H, m), 7.16 (1H, dd, J=8.1 Hz, 3.0 Hz), 7.17-7.16 (3H, m), 4.39 (1H, d, J=3.5 Hz), 4.24-3.98 (4H, m), 3.43-3.42 (4H, m), 3.43 (1.5H, s), 3.42 (1.5H, s), 3.39 (1.5H, s), 3.38 (1.5H, s), 2.57-2.45 (2H, m), 2.57-2.45 (1H, m), 1.96-1.86 (1H, m), 1.27 (3H, dt, J=6.9 Hz, 2.1 Hz).

Example 179

Ethyl (2S,3S)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(methoxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate



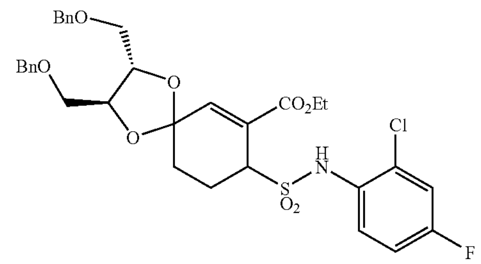
Following the process described in Example (17a), 1,4-di-O-methyl-2,3-di-O-trimethylsilyl-L-threitol was used in place of 1,4-di-o-benzoyl-2,3-di-O-trimethylsilyl-D-threitol to give the title compound as a colorless oil (91% yield).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.68-7.64 (1H, m), 7.16 (1H, dd, J=7.8 and 2.4 Hz), 7.04-7.00 (2H, m), 6.89 (1H, s), 4.40-4.39 (1H, m), 4.23-3.97 (4H, m), 3.62-3.47 (4H, m), 3.43 (1.5H, s), 3.41 (1.5H, s), 3.39 (1.5H, s), 3.38 (1.5H, s), 2.58-2.45 (2H, m), 2.26-2.16 (1H, m), 1.96-1.86 (1H, m), 1.26 (3H, dt, J=7.0 and 3.5 Hz).

Example 180

Ethyl (2S,3S)-2,3-bis(benzyloxymethyl)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate



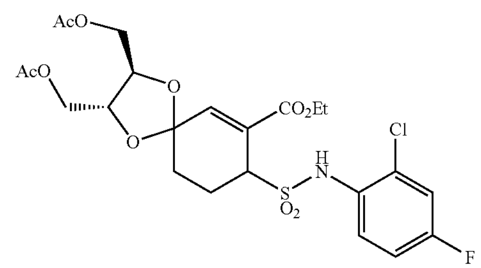
Following the process described in Example (17a), 1,4-di-O-benzyl-2,3-di-o-trimethylsilyl-L-threitol was used in place of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-D-threitol to give the title compound as a colorless oil (yield: 94%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.69-7.64 (1H, m), 7.37-7.26 (10H, m), 7.16 (1H, dd, J=7.8 Hz, 2.8 Hz), 7.04-6.90 (3H, m), 4.64-4.51 (4H, m), 4.40 (1H, t, J=4.5 Hz), 4.30-4.05 (4H, m), 3.68-3.57 (4H, m), 2.58-2.45 (2H, m), 2.25-2.17 (1H, m), 1.96-1.86 (1H, m), 1.21 (3H, dt, J=7.0 Hz, 3.5 Hz).

Example 181

Ethyl (2R,3R)-2,3-bis(acetoxymethyl)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate



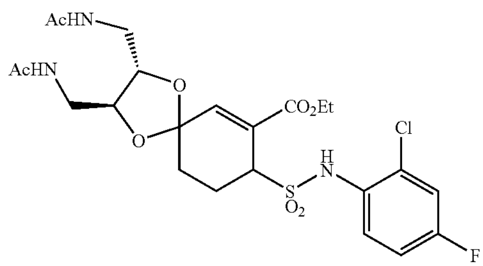
Following the process described in Example (17a), 1,4-di-O-acetyl-2,3-di-O-trimethylsilyl-D-threitol obtained in Reference Example 24 was used in place of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-D-threitol to give the title compound as a white amorphous substance (50% yield).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.67 (1H, dd, J=9.2 Hz, 5.3 Hz), 7.17 (1H, dd, J=7.9 Hz, 2.8 Hz), 7.05-7.00 (2H, m), 6.90-6.76 (1H, m), 4.41 (1H, d, J=4.7 Hz), 4.37-4.37 (8H, m), 2.60-2.46 (2H, m), 2.23-2.04 (8H, m), 1.26 (3H, t, J=7.0 Hz).

Example 182

Ethyl (2S,3S)-2,3-bis(acetylaminomethyl)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-410)



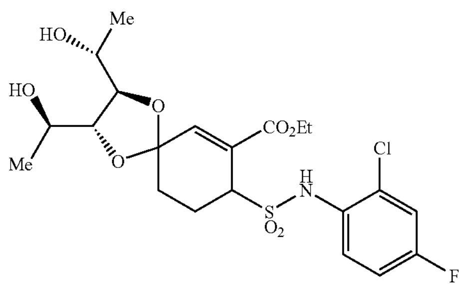
218 mg (1.07 mmol) of N-(4-acetylamino-2R,3R-dihydroxybutyl)acetamide and 0.57 ml (3.20 mmol) of isopropoxytrimethylsilane were dissolved in 3 ml of nitromethane, and 13 μl (0.071 mmol) of trimethylsilyl trifluoromethanesulfonate and 300 mg (0.711 mmol) of ethyl 6-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-dimethoxy-1-cyclohexene-1-carboxylate obtained in Example (16a) were sequentially added thereto with stirring under ice-cooling, followed by stirring for 3 hours at the same temperature and then for 116 hours at room temperature. To the reaction solution was added saturated aqueous sodium hydrogencarbonate and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; ethyl acetate methanol=9:1) to give 203 mg of the title compound as an amorphous substance (yield: 51%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.68-7.63 (1H, m), 7.20-7.15 (1H, m), 7.08-7.00 (2H, m), 6.78-6.73 (1H, m), 6.46-6.38 (1H, m), 6.34-6.26 (1H, m), 4.42-4.39 (1H, m), 4.29-4.14 (2H, m), 3.96-3.85 (1.5H, m), 3.75-3.69 (0.5H, m), 3.61-3.42 (4H, m), 2.55-2.43 (2H, m), 2.21-2.01 (7H, m), 1.90-1.78 (1H, m), 1.31-1.25 (3H, m).

Example 183

Ethyl (2R,3R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis((R)-1-hydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2163)



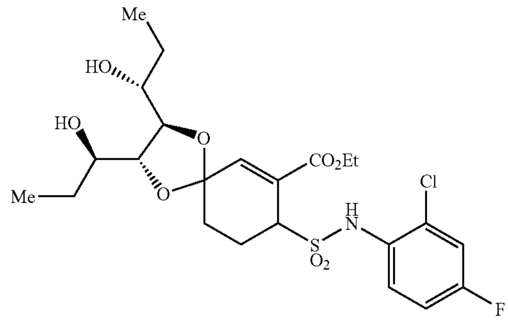
Following the process described in Example 17 (alternative procedure), (1R,2R,3R,4R)-4-benzoyloxy-1-methyl-2,3-bis[(trimethylsilyl)oxy]pentyl benzoate obtained in Reference Example 25 was used in place of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-D-threitol to give the title compound as a white amorphous substance (yield: 33%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.66 (1H, dd, J=9.0 and 5.0 Hz), 7.17 (1H, dd, J=7.8 and 2.7 Hz), 7.09 (1H, d, J=9.0 Hz), 7.05-7.00 (1H, m), 6.80 (0.5H, s), 6.76 (0.5H, s), 4.39 (1H, d, J=5.4 Hz), 4.27-4.09 (2H, m), 3.88-3.56 (4H, m), 2.50-2.42 (2H, m), 2.19-2.11 (1H, m), 1.85-1.79 (1H, m), 1.33 (3H, t, J=5.3 Hz), 1.27 (6H, t, J=7.0 Hz).

Example 184

Ethyl (2R,3R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis((R)-1-hydroxypropyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2164)



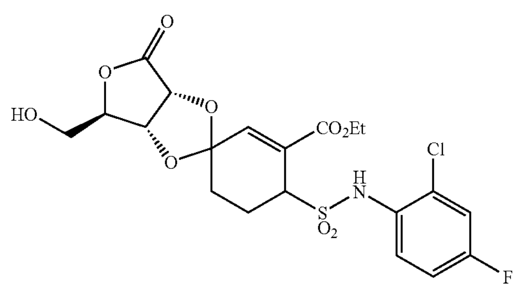
Following the process described in Example 17 (alternative procedure), (1R,2R,3R,4R)-4-benzoyloxy-1-ethyl-2,3-bis[(trimethylsilyl)oxy]hexyl benzoate obtained in Reference Example 26 was used in place of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-D-threitol to give the title compound as a white amorphous substance (yield: 21%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.68 (1H, dd, J=9.2 Hz, 5.2 Hz), 7.18 (1H, dd, J=7.4 Hz, 2.4 Hz), 7.06-7.01 (2H, m), 6.81 (0.5H, s), 6.78 (0.5H, s), 4.40 (1H, d, J=5.1 Hz), 4.29-4.12 (2H, m), 3.88-3.55 (4H, m), 3.03 (1H, brs), 2.92 (1H, brs), 2.51-2.41 (2H, m), 2.21-2.13 (2H, m), 1.90-1.73 (1H, m), 1.55-1.43 (3H, m), 1.29 (3H, t, J=7.2 Hz), 1.05-0.97 (6H, m).

Example 185

Ethyl (3a'R,6a'R,6'R)-4-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-6'-hydroxymethyl-4'-oxo-3a',4',6',6a'-tetrahydrospiro[cyclohex-2-ene-1,2'-furo[3.4-d][1.3]dioxol]-3-carboxylate (Exemplified compound No. 1-2165)



Following the process described in Example (17a), (3R,4R,5R)-3,4-bis[(trimethylsilyl)oxy]-5-[(trimethylsilyl)oxy]

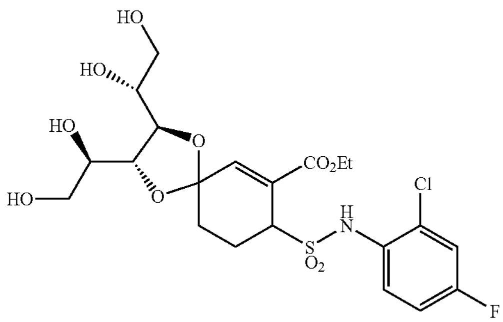
methyldihydrofuran-2-one was used in place of 1,4-di-O-benzoyl-2,3-di-O-trimethylsilyl-D-threitol to give the title compound as a white amorphous substance (yield: 25%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.69-7.64 (1H, m), 7.20-7.16 (1H, m), 7.06-6.96 (2H, m), 6.82-6.68 (1H, m), 5.04-4.62 (3H, m), 4.44-4.40 (1H, m), 4.26-4.14 (2H, m), 4.05-3.98 (1H, m), 3.90-3.81 (1H, m), 2.74-2.46 (2H, m), 2.24-2.12 (1H, m), 1.97-1.83 (2H, m), 1.30-1.26 (3H, m).

Example 186

Ethyl (2R,3R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis((1R)-1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (low polarity compound, first peak), (high polarity compound, second peak) (Exemplified compound No. 1-386)



Ethyl (2R,3R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis((1R)-1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 23 was subjected to high performance liquid chromatography (column; CHIRALPAK AD-H, size; inner diameter 2 cm, length 25 cm, solvent; hexane:2-propanol) to separate and purify two optical isomers, and low polarity compound (first peak) and high polarity compound (second peak) were respectively obtained as a white amorphous substance. According to the result of HPLC analysis of the two optical isomers obtained under the conditions below, their optical purities were respectively >99% ee.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 7:3
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 7.3 minutes high polarity compound (second peak): 9.9 minutes

(Low Polarity Compound, First Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.65 (1H, dd, J=9 Hz, 5 Hz), 7.21 (1H, bs), 7.17 (1H, dd, J=8 Hz, 3 Hz), 7.06-6.99 (1H, m), 6.80 (1H, s), 4.38 (1H, d, J=5 Hz), 4.27-4.12 (4H, m), 4.08 (2H, d, J=7 Hz), 3.95-3.88 (1H, m), 3.87-3.64 (5H, m), 2.98-2.68 (2H, m), 2.54-2.42 (2H, m), 2.22-2.08 (1H, m), 1.91-1.82 (1H, m), 1.25 (3H, t, J=7 Hz).

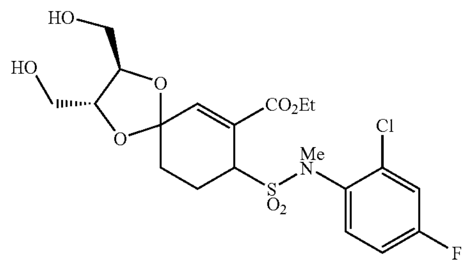
(High Polarity Compound, Second Peak)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.63 (1H, dd, J=9 Hz, 5 Hz), 7.15 (1H, bs), 7.12 (1H, dd, J=8 Hz, 3 Hz), 7.05-6.97 (1H, m), 6.76 (1H, s), 4.37 (1H, d, J=6 Hz), 4.27-4.01 (5H, m), 3.97-3.86 (2H, m), 3.85-3.45 (5H, m), 2.77-2.57 (2H, m), 2.52-2.41 (2H, m), 2.21-2.08 (1H, m), 1.89-1.80 (1H, m), 1.26 (3H, t, J=7 Hz).

Example 187

Ethyl-(2R,3R)-8-[N-(2-chloro-4-fluorophenyl)-N-methylsulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified Compound No. 2-15)



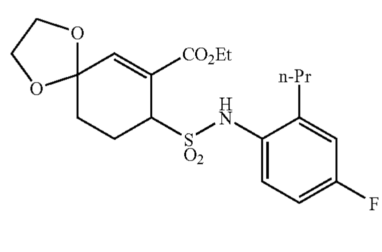
235 mg (0.49 mmol) of ethyl (2R,3R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 17 was dissolved in 1.5 ml of acetone, and 84 mg (0.59 mmol) of methyl iodide and 138 mg (1.00 mmol) of potassium carbonate were added sequentially, followed by stirring for 3 hours at 50° C. After the reaction solution was filtered, the filtrate was concentrated under reduced pressure, and the residue was subjected to silica gel column chromatography (solvent; hexane ethyl acetate=1:3) to give 175 mg of the title compound as a white amorphous substance (yield: 73%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.57 (1H, brs), 7.22 (1H, dd, J=8 Hz, 3 Hz), 7.05-7.00 (1H, m), 6.87 (0.5H, s), 6.79 (0.5H, s), 4.58 (1H, brs), 4.28-3.73 (8H, m), 3.25 (3H, s), 2.60-1.80 (6H, m), 1.26 (3H, t, J=7 Hz).

Example 188

Ethyl 8-[N-(4-fluoro-2-propylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified compound No. 1-2077)



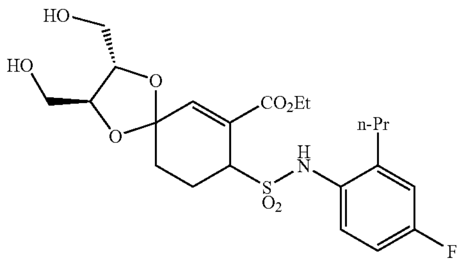
Following the process described in Example (id), 4-fluoro-2-propylphenylamine obtained in Reference Example 27 was used in place of 2-chloro-4-fluoroaniline to give the title compound as an oil (yield: 84%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

8.09-8.07 (4H, m), 7.59-7.55 (2H, m), 7.47-7.43 (4H, m), 7.47-7.43 (2H, m), 3.96 (2H, s), 2.00-1.79 (4H, m), 1.02 (6H, t, J=7 Hz), 0.07 (18H, s).

Example 189

Ethyl (2S,3S)-8-[N-(4-fluoro-2-propylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified Compound No. 1-2095)



Following the process described in Examples 7, (16a) and 18 (alternative procedure), ethyl 8-[N-(4-fluoro-2-propylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 188 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as a white amorphous substance (38% yield). This compound was separable into two optical isomers in accordance with the following HPLC conditions.

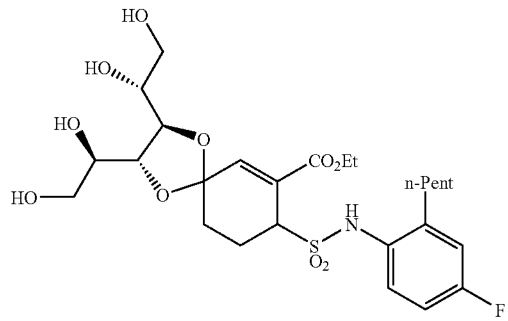
HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 4:1
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 9.6 minutes high polarity compound (second peak): 14.1 minutes

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.51-7.47 (1H, m), 6.97-6.88 (3H, m), 6.70 (0.5H, s), 6.64 (0.5H, s), 4.42-4.39 (1H, m), 4.28-3.72 (8H, m), 2.75-2.61 (2H, m), 2.52-2.37 (2H, m), 2.19-1.87 (4H, m), 1.68-1.57 (2H, m), 1.32-1.28 (3H, m), 0.99 (3H, t, J=8 Hz).

Example 190

Ethyl (2R,3R)-2,3-bis((1R)-1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified Compound No. 1-1748)



Following the process described in Examples 7, (16a) and 23, ethyl 8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 86 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as a white powder (yield: 33%). This compound was separable into two optical isomers in accordance with the following HPLC conditions.

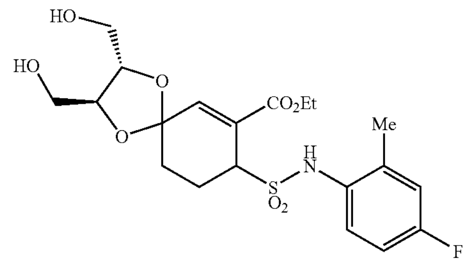
HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 7:3
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 5.29 minutes high polarity compound (second peak): 5.82 minutes

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49-7.44 (1H, m), 6.97-6.86 (2H, m), 6.84 (0.5H, m), 6.82 (0.5H, m), 6.73 (0.5H, s), 6.69 (0.5H, s), 4.41-4.36 (1H, m), 4.27-4.17 (2H, m), 4.12-4.01 (1.5H, m), 3.97-3.88 (1.5H, m), 3.88-3.67 (5H, m), 2.77-2.60 (2H, m), 2.50-2.30 (2H, m), 2.20-1.40 (8H, m), 1.39-1.25 (7H, m), 0.93-0.86 (3H, m).

Example 191

Ethyl (2S,3S)-8-[N-(4-fluoro-2-methylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate (Exemplified Compound No. 1-2359)



Following the process described in Examples 7, (16a) and 18 (alternative procedure), ethyl 8-[N-(4-fluoro-2-methylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate obtained in Example 79 was used in place of ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate to give the title compound as an amorphous substance (yield: 49%). This compound was separable into two optical isomers in accordance with the following HPLC conditions.

HPLC conditions	
Column	CHIRALPAK AD-H (produced by Daicel Chemical Industries, Ltd. inner diameter 0.46 cm, length 25 cm)
Mobile phase	hexane:2-propanol = 4:1
Flow rate	1.0 ml/min
Temperature	40° C.
Detection	254 nm (UV)
Retention time	low polarity compound (first peak): 13.5 minutes high polarity compound (second peak): 19.6 minutes

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.49 (1H, dd, J=8.8 Hz, 5.3 Hz), 6.96-6.88 (3H, m), 6.70 (0.5H, brs), 6.64 (0.5H, brs), 4.40-4.37 (1H, m), 4.28-3.70 (8H, m), 2.51-2.32 (5H, m), 2.21-1.87 (2H, m), 1.31-1.27 (3H, m).

REFERENCE EXAMPLES

Reference Example 1

1,4-Di-O-benzoyl-2,3-di-O-trimethylsilyl-meso-erythritol

300 mg (0.90 mmol) of 1,4-di-O-benzoyl-meso-erythritol (compound described in J. Am. Chem. Soc., 82, 2585 (1960)), 0.28 ml (1.98 mmol) of triethylamine and 11 mg (0.09 mmol) of 4-dimethylaminopyridine were dissolved in 6 ml of dichloromethane, and 0.24 ml (1.89 mmol) of trimethylsilyl chloride was added thereto with stirring under ice-cooling, followed by stirring for 2 hours at the same temperature. To the reaction solution was added saturated aqueous sodium hydrogencarbonate and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; ethyl acetate alone) to give 418 mg of the title compound as a white powder (yield: 98%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

8.04 (4H, d, J=7 Hz), 7.55 (2H, t, J=7 Hz), 7.43 (4H, t, J=7 Hz), 4.53 (2H, dd, J=12 Hz, J=3 Hz), 4.36 (2H, dd, J=12 Hz, 5 Hz), 4.13-4.08 (2H, m) 0.13 (18H, s)

Reference Example 2

1,3,4,5,7-Penta-O-trimethylsilyl-D-arabitol

Following the process described in Reference Example 1, D-arabitol was used in place of 1,4-di-o-benzoyl-meso-erythritol to give the title compound as a colorless oil (yield: 26%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

3.84-3.80 (1H, m), 3.76-3.68 (3H, m), 3.63-3.54 (2H, m), 3.49 (1H, dd, J=10 Hz, J=7 Hz), 0.14-0.09 (45H, m).

Reference Example 3

1,6-Di-O-benzoyl-2,3,4,5-tetra-O-trimethylsilyl-D-mannitol

Following the process described in Reference Example 1, 1,6-di-O-benzoyl-D-mannitol was used in place of 1,4-di-O-benzoyl-meso-erythritol to give the title compound as a pale brown oil (yield: 98%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

8.05 (4H, d, J=7 Hz), 7.55 (2H, t, J=7 Hz), 7.43 (4H, t, J=7 Hz), 4.59 (2H, dd, J=12 Hz, 2 Hz), 4.38-4.31 (2H, m), 4.24-4.20 (2H, m), 3.83 (2H, br.s), 0.17 (18H, s), 0.11 (18H, s).

Reference Example 4

2-Trimethylsilyloxy-1-trimethylsilyloxymethylethyl adamantane-1-carboxylate

(4a) 2-Phenyl[1.3]dioxan-5-ol adamantane-1-carboxylate

1.00 g (5.55 mmol) of 2-phenyl[1.3]dioxan-5-ol, 1.16 ml (8.32 mmol) of triethylamine and 68 mg (0.56 mmol) of 4-dimethylaminopyridine were dissolved in 20 ml of dichloromethane, and 1.28 g (6.10 mmol) of 1-adamantanecarbonyl chloride was added thereto with stirring under ice-cooling, followed by stirring for 30 minutes at the same temperature, and then further for 15 hours at room temperature. Dichloromethane was distilled off under reduced pressure, and to the residue was added aqueous sodium hydrogencarbonate and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=9:1) to give 1.52 g of the title compound as a pale yellow powder (yield: 80%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.52-7.48 (2H, m), 7.42-7.33 (3H, m), 5.54 (1H, s), 4.68-4.66 (1H, m), 4.26-4.22 (2H, m), 4.18-4.13 (2H, m), 2.07-2.01 (3H, m), 2.01-1.97 (6H, m), 1.77-1.69 (6H, m).

(4b) 2-Hydroxy-1-hydroxymethylethyl adamantane-1-carboxylate

400 mg (1.17 mmol) of 2-phenyl[1.3]dioxan-5-yl adamantane-1-carboxylate obtained in (4a) was dissolved in 8 ml of

ethyl acetate and 400 mg of 20% palladium hydroxide-carbon (water content: 50%) was added thereto, followed by stirring for 4 hours under hydrogen atmosphere at room temperature. After the catalyst was filtered, the filtrate was concentrated under reduced pressure to give 294 mg of the title compound as a white powder (yield: 99%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.90-4.85 (1H, m), 3.84-3.76 (4H, m), 2.16-2.00 (5H, m), 1.94-1.87 (6H, m), 1.78-1.67 (6H, m).

(4c) 2-Trimethylsilyloxy-1-trimethylsilyloxymethylethyl adamantane-1-carboxylate

Following the process described in Reference Example 1, 2-hydroxy-1-hydroxymethylethyl adamantane-1-carboxylate obtained in (4b) was used in place of 1,4-di-O-benzoyl-meso-erythritol to give the title compound as a colorless oil (yield: 70%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.85-4.79 (1H, m), 3.72-3.61 (4H, m), 2.04-1.97 (3H, m), 1.92-1.83 (6H, m), 1.76-1.65 (6H, m), 0.11 (18H, s).

Reference Example 5

Diethyl 2,2-bis[(trimethylsilyl)oxy]methylmalonate

Following the process described in Reference Example 1, diethyl 2,2-bis(hydroxymethyl)malonate was used in place of 1,4-di-O-benzoyl-meso-erythritol to give the title compound as a colorless oil (yield: 75%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.17 (4H, q, J=7 Hz), 4.04 (4H, s), 1.23 (6H, t, J=7 Hz), 0.07 (18H, s).

Reference Example 6

2-Pentyl-1H-pyrrol-1-ylamine

(6a) (2E)-4-Oxo-2-nonenal

2.0 g (14.47 mmol) of 2-pentylfuran was dissolved in 60 ml of dichloromethane, and 3.84 g (14.47 mmol) of 65% m-chloroperbenzoic acid was added dropwise thereto with stirring under ice-cooling, followed by stirring for 1 hour at the same temperature. To the reaction solution was added saturated aqueous sodium carbonate and the mixture was extracted with dichloromethane. The organic layer was washed with water, dried over anhydrous magnesium sulfate, and was then concentrated under reduced pressure to give 1.62 g of the title compound as a yellow oil (yield: 73%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

10.23 (1H, d, J=7 Hz), 6.95 (1H, d, J=12 Hz), 6.18 (1H, dd, J=12 Hz, 7 Hz), 2.26 (2H, t, J=7 Hz), 1.73-1.61 (2H, m), 1.40-1.26 (4H, m), 0.91 (3H, t, J=6 Hz).

(6b) 4-Oxononanal

1.62 g (10.5 mmol) of (2E)-4-oxo-2-nonenal obtained in (6a) was dissolved in 30 ml of ethyl acetate, and 160 mg of 10% palladium-carbon (water content: 50%) was added thereto, followed by restirring for 2 hours under hydrogen atmosphere at room temperature. After the catalyst was filtered, the filtrate was concentrated under reduced pressure to give 1.50 g of the title compound as a pale yellow oil (91% yield).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

9.81 (1H, s), 2.81-2.67 (4H, m), 2.47 (2H, t, J=7 HZ), 1.67-1.53 (2H, m), 1.38-1.21 (4H, m), 0.89 (3H, t, J=7 Hz).

(6c) Benzyl 2-pentyl-1H-pyrrol-1-ylcarbamate

1.50 g (9.60 mmol) of 4-oxononanal obtained in (6b) was dissolved in 45 ml of ethanol-acetic acid (2:1) solution mixture, and 1.60 g (9.60 mmol) of benzyl hydrazinecarboxylate was added thereto, followed by stirring for 1 hour at 80° C. The reaction solution was concentrated under reduced pressure, and the residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=2:1) to give 2.12 g of the title compound as a yellow oil (77% yield).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.36 (5H, bs), 7.21 (1H, ds), 6.63-6.59 (1H, m), 6.07 (1H, t, J=4 Hz), 5.89-5.84 (1H, m), 5.22 (2H, ds), 2.46-2.36 (2H, m), 1.63-1.49 (2H, m), 1.37-1.22 (4H, m), 0.88 (3H, t, J=7 Hz).

(6d) 2-Pentyl-1H-pyrrole-1-amine

1.0 g (3.49 mmol) of benzyl 2-pentyl-1H-pyrrol-1-ylcarbamate obtained in (6c) was dissolved in 20 ml of ethanol, and 100 mg of 10% palladium-carbon (water content: 50%) was added thereto, followed by stirring for 2 hours under hydrogen atmosphere at room temperature. After the catalyst was filtered, the filtrate was concentrated under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=2:1) to give 430 mg of the title compound as a yellow oil (yield: 81%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

6.68 (1H, m), 5.97 (1H, t, J=3 Hz), 5.82-5.77 (1H, m), 4.52 (2H, s), 2.58 (2H, t, J=8 Hz), 1.69-1.57 (2H, m), 1.44-1.31 (4H, m), 0.91 (3H, t, J=7 Hz).

Reference Example 7

2-Hexyl-1H-pyrrol-1-ylamine

Following the procedure described in Reference Example 6, 2-hexylfuran was used as the starting material in place of 2-pentylfuran to give the title compound as a yellow oil (yield: 29%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

6.67-6.63 (1H, m), 5.99-5.94 (1H, m), 5.81-5.77 (1H, m), 4.52 (2H, br.s), 2.62-2.55 (2H, m), 1.67-1.56 (2H, m), 1.44-1.21 (6H, m), 0.89 (3H, t, J=7 Hz).

Reference Example 8

2-Heptyl-1H-pyrrol-1-ylamine

Following the procedure described in Reference Example 6, 2-heptylfuran was used as the starting material in place of 2-pentylfuran to give the title compound as a pale yellow solid (yield: 59%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

6.67-6.63 (1H, m), 5.99-5.94 (1H, m), 5.81-5.77 (1H, m), 4.52 (2H, br.s), 2.62-2.55 (2H, m), 1.67-1.53 (2H, m), 1.44-1.21 (8H, m), 0.89 (3H, t, J=7 Hz).

Reference Example 9

2-Octyl-1H-pyrrol-1-ylamine

Following the procedure described in Reference Example 6, 2-octylfuran was used as the starting material in place of 2-pentylfuran to give the title compound as a yellow oil (yield: 11%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

6.65-6.61 (1H, m), 5.97-5.93 (1H, m), 5.78-5.75 (1H, m), 4.51 (2H, br.s), 2.60-2.55 (2H, m), 1.66-1.54 (2H, m), 1.42-1.21 (10H, m), 0.88 (3H, t, J=7 Hz).

Reference Example 10

2-Cyclopropyl-1H-pyrrol-1-ylamine

(10a) 4-Cyclopropyl-4-oxobutanal

230 mg (1.79 mmol) of 1-cyclopropyl-4-hydroxy-1-butanone was dissolved in 7 ml of dichloromethane, and 580 mg (2.69 mmol) of pyridinium chlorochromate was added thereto, followed by stirring for 1 hour at room temperature. To the reaction solution was added diethyl ether, the mixture was filtered using Celite, and the filtrate was concentrated under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; diethyl ether alone) to give 176 mg of the title compound as a pale yellow oil (yield: 78%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

9.78 (1H, s), 2.91 (2H, t, J=7 Hz), 2.78-2.71 (2H, m), 2.01-1.93 (1H, m), 1.08-1.01 (2H, m), 0.96-0.88 (2H, m).

(10b) 2-Cyclopropyl-1H-pyrrol-1-ylamine

Following the procedures described in Reference Examples (6c) and (6d), 4-cyclopropyl-4-oxobutanal obtained in (10a) was used in place of 4-oxononanal to give the title compound as a pale yellow oil (yield: 45%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

6.70-6.64 (1H, m), 5.94-5.88 (1H, m), 5.71-5.64 (1H, m), 4.69 (2H, br.s), 1.83-1.72 (1H, m), 0.91-0.83 (2H, m), 0.64-0.57 (2H, m).

Reference Example 11

4-Fluoro-2-heptylphenylamine

(11a) 4-Fluoro-2-(hept-1-enyl)-1-nitrobenzene

3.0 g (7.0 mmol) of hexyltriphenylphosphonium bromide was suspended in 30 ml of tetrahydrofuran, and 4.5 ml (7.0 mmol) of n-butyl lithium/hexane solution (1.56 M) was added dropwise thereto at −10° C. After the reaction solution was stirred for 10 minutes at the same temperature, 846 mg (5.0 mmol) of 4-fluoro-2-nitrobenzaldehyde was added, and the reaction solution was further stirred for 1 hour. To the reaction solution was added 1N aqueous potassium hydrogensulfate and the mixture was extracted with ethyl acetate. The organic layer was washed sequentially with saturated aqueous sodium hydrogencarbonate and water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=19:1) to give 917 mg of the title compound as a pale yellow oil (yield: 77%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

8.09 (1.7H, dd, J=9 Hz, 5 Hz), 7.97 (1H, dd, J=9 Hz, 5 Hz), 7.26-6.99 (5.4H, m), 6.89 (1H, d, J=16 Hz), 6.69 (1.7H, d, J=11 Hz), 6.26 (1H, dt, J=16 Hz, 7 Hz), 5.87 (1.7H, dt, J=12 Hz, 8 Hz), 2.28 (2H, q, J=7 Hz), 2.10 (3.4H, q, J=7 Hz), 1.52-1.23 (16.2H, m), 0.91 (3H, m), 0.86 (5.1H, m).

(11b) 4-Fluoro-2-heptylphenylamine

910 mg (3.8 mmol) of 4-fluoro-2-(hept-1-enyl)-1-nitrobenzene obtained in (11a) was dissolved in 5 ml of ethanol, and 100 mg of 10% palladium-carbon (water content: 50%) was added thereto, followed by stirring for 2 hours under hydrogen atmosphere at room temperature. After the catalyst was filtered, the filtrate was concentrated under reduced pressure, and the residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=9:1) to give 730 mg of the title compound as a pale yellow oil (yield: 91%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

6.80-6.71 (2H, m), 6.61 (1H, dd, J=9 Hz, 5 Hz), 3.47 (2H, brs), 2.45 (2H, t, J=7 Hz), 1.64-1.58 (2H, m), 1.42-1.24 (8H, m), 0.89 (3H, t, J=6 Hz).

Reference Example 12

2-Butyl-4-fluorophenylamine

Following the procedure described in Reference Example 11, propyltriphenylphosphonium bromide was used in place of hexyltriphenylphosphonium bromide to give the title compound as a brown oil (yield: 78%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

6.80-6.69 (2H, m), 6.60 (1H, dd, J=9 Hz, 5 Hz), 3.51 (2H, bs), 2.46 (2H, t, J=8 Hz), 1.63-1.56 (2H, m), 1.45-1.37 (2H, m), 0.96 (3H, t, J=7 Hz).

Reference Example 13

4-Fluoro-2-pentylphenylamine

Following the procedure described in Reference Example 11, butyltriphenylphosphonium bromide was used in place of hexyltriphenylphosphonium bromide to give the title compound as a yellow oil (yield: 78%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

6.80-6.69 (2H, m), 6.60 (1H, dd, J=9 Hz, 5 Hz), 3.50 (2H, bs), 2.45 (2H, t, J=8 Hz), 1.64-1.58 (2H, m), 1.45-1.36 (4H, m), 0.91 (3H, t, J=7 Hz).

Reference Example 14

4-Fluoro-2-hexylphenylamine

Following the procedure described in Reference Example 11, pentyltriphenylphosphonium bromide was used in place of hexyltriphenylphosphonium bromide to give the title compound as a pale brown oil (yield: 63%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

6.81-6.71 (2H, m), 6.66 (1H, dd, J=9 Hz, 5 Hz), 4.19 (2H, brs), 2.48 (2H, t, J=8 Hz), 1.65-1.57 (2H, m), 1.43-1.25 (6H, m), 0.92-0.85 (3H, m).

Reference Example 15

4-Fluoro-2-octylphenylamine

Following the procedure described in Reference Example 11, heptyltriphenylphosphonium bromide was used in place of hexyltriphenylphosphonium bromide to give the title compound as a pale yellow oil (yield: 65%)

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

6.80-6.71 (2H, m), 6.61 (1H, dd, J=9 Hz, 5 Hz), 2.45 (2H, t, J=7 Hz), 1.64-1.56 (2H, m), 1.38-1.22 (10H, m), 0.88 (3H, t, J=7 Hz).

Reference Example 16

4-Fluoro-2-nonylphenylamine

Following the procedure described in Reference Example 11, octyltriphenylphosphonium bromide was used in place of

hexyltriphenylphosphonium bromide to give the title compound as a pale brown oil (yield: 97%).

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

6.77 (1H, dd, J=10 Hz, 3 Hz), 6.72 (1H, td, J=8 Hz, 3 Hz), 6.59 (1H, dd, J=9 Hz, 5 Hz), 3.46 (2H, brs), 2.45 (2H, t, J=8 Hz), 1.64-1.56 (2H, m), 1.44-1.21 (12H, m), 0.88 (3H, t, J=7 Hz).

Reference Example 17

2-Decyl-4-fluorophenylamine

Following the procedure described in Reference Example 11, nonyltriphenylphosphonium bromide was used in place of hexyltriphenylphosphonium bromide to give the title compound as a pale brown oil (yield: 67%).

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm:

6.77 (1H, dd, J=10 Hz, 3 Hz), 6.73 (1H, dd, J=8 Hz, 3 Hz), 6.60 (1H, dd, J=9 Hz, 5 Hz), 3.47 (2H, brs), 2.45 (2H, t, J=8 Hz), 1.64-1.56 (2H, m), 1.43-1.21 (14H, m), 0.88 (3H, t, J=7 Hz).

Reference Example 18

1,4-Di-O-benzoyl-2,3-di-o-trimethylsilyl-D-threitol

17.48 g (52.9 mmol) of 1,4-di-C-benzoyl-D-threitol and 10.8 g (159 mmol) of imidazol were dissolved in 250 ml of dichloromethane, and 12.6 g (116 mmol) of chlorotrimethylsilane was added thereto with stirring under ice-cooling, followed by stirring for 1 hour at room temperature. The reaction solution was directly subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=20:1-5:1) to give 24.59 g of f the title compound as a white powder (yield: 98%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

8.04 (4H, dd, J=8 Hz, J=1 Hz), 7.57-7.52 (2H, m), 7.46-7.40 (4H, m), 4.50 (2H, dd, J=11 Hz, J=4 Hz), 4.48-4.33 (2H, m), 4.13-4.08 (2H, m), 0.14 (18H, s).

Reference Example 19

1,4-Di-O-benzoyl-2,3-di-O-trimethylsilyl-L-threitol

Following the process described in Reference Example 18, 1,4-di-O-benzoyl-L-threitol was used in place of 1,4-di-o-benzoyl-D-threitol to give the title compound as a white powder (yield: 98%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

8.04 (4H, dd, J=8 Hz, J=1 Hz), 7.57-7.52 (2H, m), 7.46-7.40 (4H, m), 4.50 (2H, dd, J=11 Hz, J=4 Hz), 4.48-4.33 (2H, m), 4.13-4.08 (2H, m), 0.14 (18H, s)

Reference Example 20

Methyl (S)-3,4-bis[(trimethylsilyl)oxy]butyrate

Following the process described in Reference Example 18, methyl (S)-3,4-dihydroxybutyrate was used in place of 1,4-di-O-benzoyl-D-threitol to give the title compound as an oil (yield: 62%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.18-4.12 (1H, m), 3.67 (3H, s), 3.52 (1H, dd, J=10 Hz, 6 Hz), 3.40 (1H, dd, J=10 Hz, 6 Hz), 2.59 (1H, dd, J=15 Hz, 5 Hz), 2.37 (1H, dd, J=15 Hz, 7 Hz), 0.10 (18H, s).

Reference Example 21

1,4-Anhydro-2,3-di-O-trimethylsilyl-meso-erythritol

Following the process described in Reference Example 1, 1,4-anhydroerythritol was used in place of 1,4-di-o-benzoyl-meso-erythritol to give the title compound as a colorless oil (yield: 21%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.15-4.10 (2H, m), 3.92-3.85 (2H, m), 3.68-3.62 (2H, m), 0.14 (18H, s).

Reference Example 22

3-Ethyl-3,4-bis[(trimethylsilyl)oxy]hexane

(22a) 3-Ethylhexane-3,4-diol

590 mg (5.0 mmol) of dimethyloxalate was dissolved in 20 ml of tetrahydrofuran, and 22 ml (22 mmol) of 1.0 M ethyl magnesium bromide/tetrahydrofuran solution was added thereto with stirring under ice-cooling, followed by stirring for 2 hours at the same temperature. The reaction solution was made acidic by addition of 1N hydrochloric acid and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=3:1) to give 276 mg of the title compound as an oil (yield: 38%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

3.45-3.41 (1H, m), 1.87 (1H, d, J=6 Hz), 1.75 (1H, s), 1.70-1.31 (6H, m), 1.04 (3H, t, J=7 Hz), 0.89 (3H, t, J=8 Hz), 0.89 (3H, t, J=8 Hz).

(22b) 3-Ethyl-3,4-bis[(trimethylsilyl)oxy]hexane

270 mg (1.85 mmol) of 3-ethylhexane-3,4-diol obtained in (22a) was dissolved in 5 ml of pyridine, and 597 mg (3.7 mmol) of 1,1,1,3,3,3-hexamethylsilazane and 1.20 g (11 mmol) of chlorotrimethylsilane were added sequentially, followed by stirring for 2 hours at the same temperature and further overnight at room temperature. To the reaction solution was added water and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulfate, followed by concentration under reduced pressure. The residue was subjected to silica gel column chromatography (solvent; hexane:ethyl acetate=9:1) to give 469 mg of the title compound as an oil (yield: 88%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

3.38 (1H, dd, J=9.0 Hz, 3.0 Hz), 1.68-1.33 (6H, m), 0.90 (3H, t, J=6.0 Hz), 0.92-0.90 (6H, m), 0.11-0.08 (18H, m).

Reference Example 23

(R)-1,2-Bis[(trimethylsilyl)oxy]-1,1,2-triphenylethane

Following the process described in Reference Example 18, (R)-1,1,2-triphenyl-1,2-ethanediol was used in place of 1,4-di-O-benzoyl-D-threitol to give the title compound as a powder (yield: 99%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

7.28-7.18 (15H, m), 5.51 (1H, s), −0.05 (9H, s), −0.16 (9H, s).

Reference Example 24

1,4-Di-O-acetyl-2,3-di-O-trimethylsilyl-D-threitol

Following the process described in Reference Example 18, 1,4-di-O-acetyl-D-threitol was used in place of 1,4-di-O-benzoyl-D-threitol to give the title compound as an oil (yield: 96%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

4.20 (2H, dd, J=11 Hz, 4 Hz), 4.01 (2H, dd, J=11 Hz, 7 Hz), 3.88-3.84 (2H, m), 2.06 (6H, s), 0.13 (18H, s).

Reference Example 25

(1R,2R,3R,4R)-4-Benzoyloxy-1-methyl-2,3-bis[(trimethylsilyl)oxy]pentyl benzoate

Following the process described in Reference Example 18, (1R,2S,3S,4R)-4-benzoyloxy-2,3-dihydroxy-1-methylpentyl benzoate was used in place of 1,4-di-O-benzoyl-D-threitol to give the title compound as an oil (yield: 86%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

8.06-8.04 (4H, m), 7.57-7.54 (2H, m), 7.46-7.42 (4H, m), 5.31-5.25 (2H, m), 3.98-3.97 (2H, m), 1.41 (6H, d, J=6 Hz), 0.12 (18H, s).

Reference Example 26

(1R,2R,3R,4R)-4-Benzoyloxy-1-ethyl-2,3-bis[(trimethylsilyl)oxy]hexyl benzoate

Following the process described in Reference Example 18, (1R,2S,3S,4R)-4-benzoyloxy-1-ethyl-2,3-dihydroxyhexyl benzoate was used in place of 1,4-di-O-benzoyl-D-threitol to give the title compound as an oil (yield: 82%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

8.09-8.07 (4H, m), 7.59-7.55 (2H, m), 7.47-7.43 (4H, m), 7.47-7.43 (2H, m), 3.96 (2H, s), 2.00-1.79 (4H, m), 1.02 (6H, t, J=7 Hz), 0.07 (18H, s).

Reference Example 27

4-Fluoro-2-propylphenylamine

Following the process described in Reference Example 11, ethyltriphenylphosphonium bromide was used in place of hexyltriphenylphosphonium bromide to give the title compound as a pale yellow oil (yield: 17%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm:

6.80-6.59 (3H, m), 3.48 (2H, brs), 2.45 (2H, t, J=7 Hz), 1.70-1.58 (2H, m), 1.01 (3H, t, J=8 Hz).

Test Examples

Test Example 1

Suppression Effect Against Endotoxin Stimulated TNF-α Production in Cells (In Vitro)

The suppression rate of the compound according to the present invention against TNF-α production when human monocyte cell line U937 was stimulated by endotoxin, was measured. Specifically, to RPMI1640 medium containing 10% (volume %) of heat-inactivated new born calf serum, was added 12-O-tetradecanoylphorbol 13-acetate so that its final concentration became 30 ng/ml. U937 cells were suspended with the medium and plated to a 96 well culture plate

(Sumilon) so that number of cells/volume was 2×10^4/0.1 ml, and were then cultured for 3 days at 37° C. in a carbon dioxide incubator with 5% CO_2 and 100% humidity. After completion of incubation, the culture supernatant was removed. The compound according to the present invention was added to each of the wells in various concentrations, and lipopolysaccharide (LPS) (*E. coli* 0111:B4, Sigma) was also added so that its final concentration was 30 ng/ml. After incubating the culture plate in the carbon dioxide incubator again for 4.5 hours, the culture supernatant was collected. By using a 384 half well black plate (Greiner) and HTRF quantitative kit of CIS Bio International, the concentration of TNF-α in the culture supernatant was measured as time-resolved fluorescence with Discovery (Packard). From the measured value in the absence of LPS (X), measured value in the absence of the compound according to the present invention (Y) and measured value in the presence of the compound according to the present invention (Z), the suppression rate of TNF-α production was obtained by the following calculation formula [I].

$$\text{Suppression rate of TNF-}\alpha\text{ production (\%)}=\{1-(Z-X)/(Y-X)\}\times100 \qquad \text{[I]}$$

In the present test, the compound according to the present invention showed an excellent suppression effect against endotoxin stimulated TNF-α production in cells.

Test Example 2

Suppression Effect Against Elevated TNF-α Concentration in Blood (In Vivo)

The suppression effect of the compound according to the present invention against elevated TNF-α concentration in blood was evaluated. The test for TNF-α concentration elevation in blood was conducted in accordance with the process of Parant et al, which is described in Journal of Leukocyte Biology, Vol. 47, p. 164 (1990).

In the test, 3 to 4 male Sprague Dawley rats (8-9 weeks old) were used for each group.

4 hours before the administration of LPS, muramyl dipeptide dissolved in a physiological saline solution (1 mg/ml) was administered to the tail vein at a rate of 1 ml/kg. 0.5 hours before the administration of LPS, the rats were anaesthetized with pentobarbital (40 mg/kg), and the compound according to the present invention dissolved in 5% dimethyl acetamide/95% polyethylene glycol 400 solution was administered to the right femoral vein at a rate of 1 ml/kg. The control group was administered with 5% dimethyl acetamide/95% polyethylene glycol 400 solution at a rate of 1 ml/kg. LPS dissolved in a physiological saline solution (3 μg/ml) was administered to the left femoral vein at a rate of 1 ml/kg. 2 hours after the administration of LPS, blood was collected using 3.8% (w/v) sodium citrate solution as an anticoagulant, and blood plasma was separated by centrifuge (10,000 g, 5 minutes, 4° C.). TNF-α concentration in the blood plasma was measured using a TNF-α quantitative kit (Bio Source International, Inc.). From the TNF-α concentration in the blood of control group (X) and the TNF-α concentration in the blood of the group administered with the compound according to the present invention (Y), the TNF-α elevation suppression rate was calculated using the following calculation formula [II].

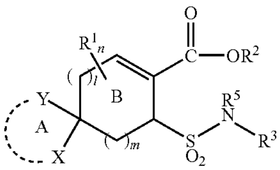
$$\text{TNF-}\alpha\text{ elevation suppression rate (\%)}=\{1-Y/X\}\times100 \qquad \text{[II]}$$

In the present test, the compound according to the present invention showed excellent suppression effects against elevated TNF-α concentration in blood.

The invention claimed is:

1. A compound represented by the general formula (I):

(I)



{wherein

X and Y represent a group in which X and Y together with the carbon atom of ring B to which they are bound form ring A, X and Y together represent a substituent of ring B, or X and Y each represents a hydrogen atom;

(1) in the case where X and Y represent a group in which X and Y together with the carbon atom of ring B to which they are bound form ring A:

ring A represents

a 3- to 7-membered heterocyclyl ring (in the heterocyclyl ring, X and Y, independently from each other, represent any one selected from a carbon atom, a group having the formula NR (R represents a hydrogen atom or a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_1-C_6 alkanoyl group which may be substituted with one or more groups selected from Substituent group α), an oxygen atom, a sulfur atom, a group having the formula SO and a group having the formula SO_2, the heterocyclyl ring may include an unsaturated bond,

may form a fused ring or spiro ring with a 3- to 7-membered heterocyclyl ring or 3- to 7-membered cycloalkyl ring, and

ring A, including the fused ring or spiro ring, may be substituted with the same or different 1 to 4 groups selected from the group consisting of an oxo group, a thioxo group, Substituent group α, a cyclopropyl C_1-C_6 alkyl group,

a C_1-C_6 alkyl group which may be substituted with 1 to 5 groups selected from Substituent group α,

a C_2-C_6 alkenyl group which may be substituted with 1 to 5 groups selected from Substituent group α, and a C_2-C_6 alkynyl group which may be substituted with 1 to 5 groups selected from Substituent group α) or

a 3- to 7-membered cycloalkyl ring (the cycloalkyl ring may include an unsaturated bond, may form a fused ring or spiro ring with a 3- to 7-membered heterocyclyl ring or 3- to 7-membered cycloalkyl ring, and

ring A, including the fused ring or spiro ring, may be substituted with the same or different 1 to 4 groups selected from the group consisting of Substituent group α, a cyclopropyl C_1-C_6 alkyl group,

a C_1-C_6 alkyl group which may be substituted with 1 to 5 groups selected from Substituent group α,

a C_2-C_6 alkenyl group which may be substituted with 1 to 5 groups selected from Substituent group α, and

a C_2-C_6 alkynyl group which may be substituted with 1 to 5 groups selected from Substituent group α);

(2) in the case where X and Y together represent a substituent of ring B:

X and Y represent an oxo group or a thioxo group;

1 and m, independently from each other, represent an integer of 0 to 3, and 1+m is 1 to 3;

R^1 represents

an aliphatic hydrocarbon group which may be substituted with one or more groups selected from Substituent group β and Substituent group γ (wherein the aliphatic hydrocarbon group represents a C_1-C_{20} alkyl group, C_3-C_{10}cycloalkyl group, C_4-C_{12} cycloalkylalkyl group, C_3-C_6 alkenyl group or C_3-C_6 alkynyl group),

a phenyl group which may be substituted with one or more groups selected from Substituent group δ,

a group having the formula OR^4 (R^4 represents a hydrogen atom or an aliphatic hydrocarbon group which may be substituted with one or more groups selected from Substituent group β and Substituent group γ, the aliphatic hydrocarbon group has the same meaning as defined above) or a halogen atom;

n represents an integer of 0 to 3;

R^2 represents a hydrogen atom,

a C_1-C_6 alkyl group which may be substituted with one or more groups selected from Substituent group β,

a C_2-C_6 alkenyl group which may be substituted with one or more groups selected from Substituent group β, or

a C_2-C_6 alkynyl group which may be substituted with one or more groups selected from Substituent group β;

R^3 represents

a phenyl group which may be substituted with one or more groups selected from Substituent group ϵ, or

a 5- or 6-membered heteroaryl group which may be substituted with one or more groups selected from Substituent group ϵ (the heteroaryl group includes 1 to 3 hetero atoms selected from a nitrogen atom, oxygen atom and sulfur atom);

R^5 represents a hydrogen atom,

a C_1-C_6 alkyl group which may be substituted with one or more groups selected from Substituent group β,

a C_2-C_6 alkenyl group which may be substituted with one or more groups selected from Substituent group β, or

a C_2-C_6 alkynyl group which may be substituted with one or more groups selected from Substituent group β;

provided that in the case where R^3 is a phenyl group which may be substituted with one or more groups selected from Substituent group ϵ, X and Y represent the aforementioned (1) or (2);

Substituent group α represents

a hydroxy group, halogen atom, C_1-C_6 alkoxy group, halogeno C_1-C_6 alkoxy group, carboxy group, C_1-C_6 alkoxycarbonyl group;

carbamoyl group which may be substituted with one or more groups selected from a C_1-C_6 alkyl group, C_2-C_6 alkenyl group, C_2-C_6 alkynyl group, C_1-C_6 alkanoyl group or C_2-C_6 alkenyl-carbonyl group;

and a group having the formula NR^6R^7, and

R^6 and R^7, independently from each other, represent a hydrogen atom, C_1-C_6 alkyl group, C_2-C_6 alkenyl group, C_2-C_6 alkynyl group, C_1-C_6 alkanoyl group or C_2-C_6 alkenyl-carbonyl group, or together with the nitrogen atom to which they are bound form a heterocyclyl group;

Substituent group β represents

an oxo group, hydroxy group, cyclopropyl group, C_1-C_6 alkoxy group, C_1-C_6 alkylthio group, nitro group, halogen atom, cyano group, carboxy group, C_1-C_{10} alkoxycarbonyl group, C_1-C_6 alkanoyl group, C_2-C_4 alkenyl-carbonyl group, C_2-C_6 alkanoyloxy group, C_2-C_4 alkenyl-carbonyloxy group;

carbamoyl group which may be substituted with one or more groups selected from a C_1-C_4 alkyl group, phenyl group, C_1-C_7 acyl group and C_1-C_4 alkoxy-phenyl group;

thiocarbamoyl group which may be substituted with a C_1-C_4 alkyl group or phenyl group;

carbamoyloxy group which may be substituted with a C_1-C_4 alkyl group or phenyl group;

C_1-C_6 alkanoylamino group, C_1-C_{10} alkoxy-carboxamide group, C_1-C_{10} alkoxy-carbonyloxy group, and

ureido group which may be substituted with a C_1-C_4 alkyl group or phenyl group;

Substituent group γ represents

a heterocyclic group, C_3-C_{10} cycloalkyloxy group, C_6-C_{10} aryloxy group, C_7-C_{19} aralkyloxy group, heterocyclyloxy group, C_3-C_{10} cycloalkylthio group, C_6-C_{10} arylthio group, C_7-C_{19} aralkylthio group, heterocyclylthio group, heterocyclylsulfinyl group, heterocyclylsulfonyl group, C_3-C_6 cycloalkyloxy-carbonyl group, C_6-C_{10} aryloxy-carbonyl group, C_7-C_{19} aralkyloxy-carbonyl group, heterocyclyloxycarbonyl group, C_6-C_{10}aryl-carbonyl group, C_6-C_{10} aryl-carbonyloxy group, C_6-C_{10} aryl-carbonylamino group, C_6-C_{10} aryloxy-carboxamide group, C_7-C_{19} aralkyloxy-carboxamide group, C_6-C_{10} aryloxy-carbonyloxy group, C_7-C_{19} aralkyloxy-carbonyloxy group, C_3-C_{10} cycloalkyloxy-carbonyloxy group and C_6-C_{10} aryl group which may be substituted with one or more groups selected from Substituent group β;

Substituent group δ represents

a hydroxy group, nitro group, cyano group, halogen atom, C_1-C_6 alkyl group, halogeno C_1-C_6 alkyl group, C_1-C_6 alkoxy group, halogeno C_1-C_6 alkoxy group, carboxy group, C_1-C_6 alkanoyl group, C_1-C_6 alkoxy-carbonyl group, C_1-C_6 alkanoylamino group, C_1-C_6 alkylthio group, carbamoyl group, C_1-C_6 alkyl-carbamoyl group, C_1-C_6 alkoxy-carbonyl C_1-C_6 alkyl-carbamoyl group, 1,3-diacylguanidino C_1-C_6 alkyl group, a group having the formula NR^6R^7 (R^6 and R^7 are the same as R^6 and R^7 of Substituent group α), C_3-C_6 cycloalkyl group, C_6-C_{10} aryl group and 5-membered heteroaryl group; and

Substituent group ϵ represents

a hydroxy group, nitro group, cyano group, halogen atom, C_1-C_{14} alkyl group, cyclopropyl C_1-C_{14} alkyl group, halogeno C_1-C_{14} alkyl group, C_1-C_{14} alkoxy group, halogeno C_1-C_{14} alkoxy group, carboxy group, C_1-C_{14} alkanoyl group, C_1-C_{14} alkoxy-carbonyl group, C_1-C_{14} alkanoylamino group, C_1-C_{14} alkylthio group, carbamoyl group, C_1-C_{14} alkyl-carbamoyl group, C_1-C_{14} alkoxy-carbonyl C_1-C_{14} alkyl-carbamoyl group, 1,3-diacylguanidino C_1-C_{14} alkyl group, group having the formula NR^6R^7 (R^6 and R^7 are the same as R^6 and R^7 of Substituent group α), C_3-C_6 cycloalkyl group, C_6-C_{10} aryl group and 5-membered heteroaryl group} or a pharmacologically acceptable salt thereof.

2. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein 1 is 0 and m is an integer of 1 to 3.

3. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein 1 is 0 and m is 2.

4. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein

X and Y together with the carbon atom of ring B form ring A, and ring A is a 3- to 7-membered heterocyclyl ring

(in the heterocyclyl ring, X and Y, independently from each other, represent any one selected from a carbon atom, a group having the formula NR (R represents a hydrogen atom or a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_1-C_6 alkanoyl group which may be substituted with one or more groups selected from Substituent group α), an oxygen atom, a sulfur atom, a group having the formula SO and a group having the formula SO_2,

the heterocyclyl ring may form a fused ring or Spiro ring with a 5- or 6-membered heterocyclyl ring (the heterocyclyl ring includes 1 or 2 oxygen and/or nitrogen atoms as hetero atoms) or 5- to 6-membered cycloalkyl ring, and

ring A, including the fused ring or Spiro ring, may be substituted with the same or different 1 to 4 groups selected from the group consisting of an oxo group, a thioxo group, Substituent group α, a cyclopropyl C_1-C_6 alkyl group and a C_1-C_6 alkyl group which may be substituted with 1 to 5 groups selected from Substituent group α) or

a 3- to 7-membered saturated cycloalkyl ring

(the 3- to 7-membered saturated cycloalkyl ring may be substituted with 1 or 2 groups selected from the group consisting of a hydroxy group, hydroxymethyl group, 1,2-dihydroxyethyl group, 1,2,3-trihydroxypropyl group, 1,2,3,4-tetrahydroxybutyl group and acetylamino group).

5. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein

X and Y represent a group in which X and Y together with the carbon atom of ring B form ring A, and ring A is

a 3- to 7-membered heterocyclyl ring

(in the heterocyclyl ring, X and Y, independently from each other, represent any one selected from a carbon atom, an oxygen atom, sulfur atom, a group having the formula SO and a group having the formula SO_2,

the heterocyclyl ring may form a fused ring or Spiro ring with a 5- or 6-membered heterocyclyl ring (the heterocyclyl ring includes 1 or 2 oxygen and/or nitrogen atoms as hetero atoms) or 5- or 6-membered cycloalkyl ring, and

ring A, including the fused ring or Spiro ring, may be substituted with the same or different 1 to 4 groups selected from the group consisting of an oxo group, a thioxo group, Substituent group α and a C_1-C_6 alkyl group which may be substituted with 1 to 4 groups selected from Substituent group α) or

a 3- to 5-membered saturated cycloalkyl ring

(the 3- to 5-membered saturated cycloalkyl ring may be substituted with 1 or 2 groups selected from the group consisting of a hydroxymethyl group, 1,2-dihydroxyethyl group, 1,2,3-trihydroxypropyl group, 1,2,3,4-tetrahydroxybutyl group and acetylamino group).

6. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein

X and Y represent a group in which X and Y together with the carbon atom of ring B form ring A, and ring A is

a 3- to 7-membered heterocyclyl ring

(the 3- to 7-membered heterocyclyl ring is oxirane, oxolane, tetrahydrofuran, tetrahydropyran, 1,3-dioxolane, 1,3-dioxane, 1,3-dioxepane, 1,3-dithiolane, 1,3-dithiane, 1,1,3,3-tetraoxo-1,3-dithiolane, 1,3-oxathiolane, 1,3-oxathiane or 1,3-oxathiepane,

these heterocyclyl rings may form a fused ring or spiro ring with a 5- or 6-membered heterocyclyl ring (the 5- or 6-membered heterocyclyl ring is tetrahydrofuran, tetrahydropyran, pyrrolidine, piperidine or 1,3-dioxane) or cyclohexyl ring, and

ring A, including the fused ring and spiro ring, may be substituted with 1 or 2 groups selected from the group consisting of an oxo group, a thioxo group, Substituent group α (Substituent group α represents a hydroxy group and a group having the formula NR^6R^7, and R6 and R^7, independently from each other, represent a hydrogen atom or C_1-C_6 alkanoyl

group), a methyl group, an ethyl group and a C_1-C_6 alkyl group which is substituted with 1 to 4 hydroxy groups), or

a cyclopropyl or cyclopentyl ring

(the cyclopropyl or cyclopentyl ring may be substituted with 1 or 2 groups selected from the group consisting of a hydroxymethyl group, 1,2-dihydroxyethyl group, 1,2,3-trihydroxypropyl group, and a 1,2,3,4-tetrahydroxybutyl group).

7. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein

X and Y represent a group in which X and Y together with the carbon atom of ring B form ring A, and ring A is

a 3- to 6-membered heterocyclyl ring

{the heterocyclyl ring is

oxirane, tetrahydrofuran,

1,3-dioxolane, 1,3-dioxane,

1,3-dithiolane, 1,3-dithiane,

1,3-oxathiolane, or 1,3-oxathiane,

these heterocyclyl rings may form a fused ring or Spiro ring with a 5- or 6-membered heterocyclyl ring (the 5- or 6-membered heterocyclyl ring is tetrahydrofuran, tetrahydropyran or 1,3-dioxane) or cyclohexyl ring, and ring A, including the fused ring or spiro ring, may be substituted with 1 or 2 groups selected from the group consisting of Substituent group α (Substituent group α represents a hydroxy group and a group having the formula NR^6R^7 (R^6 and R^7, independently from each other, represent a hydrogen atom or acetyl group), a methyl group, an ethyl group, a hydroxymethyl group, a 1,2-dihydroxyethyl group, a 1,2,3-trihydroxypropyl group and a 1,2,3,4-tetrahydroxybutyl group}.

8. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein

n is 0 or 1, and

R^1 is a hydroxy group, halogen atom, C_1-C_6 alkyl group or C_1-C_6 alkoxy group.

9. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein

n is 0 or 1, and

R^1 is a fluorine atom or methyl group.

10. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein n is 0.

11. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein R^2 is a C_1-C_6 alkyl group.

12. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein R^2 is a C_1-C_4 alkyl group.

13. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein R^2 is an ethyl group.

14. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein

R^3 is

a phenyl group which may be substituted with one or more groups selected from Substituent group ε, or

a pyrrolyl group which may be substituted with one or more groups selected from Substituent group ε, and

Substituent group ε is a halogen atom, C_1-C_{14} alkyl group and halogeno C_1-C_{14} alkyl group.

15. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein

R^3 is

a phenyl group which may be substituted with one or more groups selected from Substituent group ε, or

a pyrrolyl group which may be substituted with one or more groups selected from Substituent group ε, and

Substituent group ε is a fluorine atom, chlorine atom, bromine atom, C_3-C_8 alkyl group and halogeno C_4-C_8 alkyl group.

16. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein

R^3 is

a phenyl group which may be substituted with one or more groups selected from Substituent group ε, and

Substituent group ε is a fluorine atom, chlorine atom and C_3-C_8 alkyl group.

17. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein R^5 is a hydrogen atom or C_1-C_6 alkyl group.

18. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein R^5 is a hydrogen atom or methyl group.

19. The compound or pharmacologically acceptable salt thereof according to claim **1**, wherein R^5 is a hydrogen atom.

20. The compounds of the following group selected from claim **1** or pharmacologically acceptable salt thereof:

ethyl 8-[N-(2-chloropheny)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloropheny)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2,4-difluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2,4-difluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-hydroxymethyl-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-4-fluoropheny)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-4-fluoropheny)sulfamoyl]-2-(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-(1,2,3-trihydroxypropyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2-(1,2,3,4-tetrahydroxybutyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(acetylaminomethyl)-8N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3-hydroxy-1,5-dioxaspiro[5.5]undec-7-ene-8-carboxylate,

ethyl 3-acetylamino-9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-1,5-dioxaspiro[5.5]undec-7-ene-8-carboxylate,

ethyl 9-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-3,3-bis(hydroxymethyl)-1,5-dioxaspiro[5.5]undec-7-ene-8-carboxylate,

ethyl 8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-butyl-4-fluoropheny)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-hexylphenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-heptylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-heptylphenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-heptylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-bromophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-bromophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-6-methylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro [4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-6-methylphenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro [4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro [4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro [4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(hydroxymethyl)-8-[N-(2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro [4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro [4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro [4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro [4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-octylphenyl)sulfamoyl]-1,4-dioxaspiro [4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(4-fluoro-2-propylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro [4.5]dec-6-ene-7-carboxylate,

ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-propylphenyl)sulfamoyl]-1,4-dioxaspiro [4.5]dec-6-ene-7-carboxylate, and

ethyl 8-[N-(2-chloro-4-fluorophenyl)-N-methylsulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate.

21. A pharmaceutical composition or pharmacologically acceptable salt thereof comprising any of the compounds according to claim **1**, and a pharmaceutically acceptable excipient.

22. A method for suppressing intracellular signal transduction or cell activation induced by, endotoxin comprising the administration of an effective amount of the pharmaceutical composition or pharmaceutically acceptable salt thereof according to claim **21**.

23. A method for suppressing the generation of inflammatory mediators due to intracellular signal transduction or cell activation induced by endotoxin comprising the administration of an effective amount of the pharmaceutical composition or pharmaceutically acceptable salt thereof according to claim **21**.

24. A method for treatment of sepsis comprising the administration of an effective amount of the pharmaceutical composition or pharmaceutically acceptable salt thereof according to claim **21**.

25. The compounds of the following group selected from claim **1** or pharmacologically acceptable salt thereof:

ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(4-fluoro-2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate,

ethyl 8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate, and

ethyl 2,3-bis(1,2-dihydroxyethyl)-8[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate.

26. The following compound selected from claim **1** or pharmacologically acceptable salt thereof: ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl) -1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate.

27. The following compound selected from claim **1** or pharmacologically acceptable salt thereof: ethyl 8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate.

28. The following compound selected from claim **1** or pharmacologically acceptable salt thereof: ethyl 8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl) -1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate.

29. The following compound selected from claim **1** or pharmacologically acceptable salt thereof: ethyl 8-[N-(2-butyl-4-fluorophenyl)sulfamoyl]-2,3-bis(1,2-dihydroxyethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate.

30. The following compound selected from claim **1** or pharmacologically acceptable salt thereof: ethyl 8-[N-(4-

fluoro-2-hexylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl) - 1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate.

31. The following compound selected from claim **1** or pharmacologically acceptable salt thereof: ethyl 8-[N-(2-bromo-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl) - 1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate

32. The following compound selected from claim **1** or pharmacologically acceptable salt thereof: ethyl 8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-2,3-bis(hydroxymethyl) - 1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate.

33. The following compound selected from claim **1** or pharmacologically acceptable salt thereof: ethyl 2,3-bis(1,2-dihydroxyethyl)-8-[N-(4-fluoro-2-pentylphenyl)sulfamoyl]-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate.

34. A pharmaceutically acceptable salt of ethyl (2R,3R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate.

35. A potassium salt of ethyl (2R,3R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4-dioxaspiro[4.5]dec-6-ene-7-carboxylate.

36. A pharmaceutical composition comprising the compound according to claim **34**, and a pharmaceutically acceptable excipient.

37. A method for treating sepsis comprising administering a pharmaceutical composition comprising the compound according to claim **34**, and a pharmaceutically acceptable excipient.

38. A pharmaceutical composition comprising the compound according to claim **35**, and a pharmaceutically acceptable excipient.

39. A method of treating sepsis comprising administering a pharmaceutical composition comprising the compound according to claim **35**, and a pharmaceutically acceptable excipient.

40. A pharmaceutically acceptable salt of ethyl (2R,3R,8R)-8-[N-(2-chloro-4-fluorophenyl)sulfamoyl]-2,3-bis(hydroxymethyl)-1,4dioxaspiro[4.5]dec-6-ene-7-carboxylate.

41. Potassium (2-chloro-4-fluorophenyl){[(2R,3R,8R)-7-(ethoxycarbonyl)-2,3-bis(hydroxymethyl)-1,4-dioxaspiro [4.5]dec-6-en-8-yl] sulfonyl}azanide.

42. A pharmaceutical composition comprising the compound according to claim **40**, and a pharmaceutically acceptable excipient.

43. A method for treating sepsis comprising administering a pharmaceutical composition comprising the compound according to claim **40**, and a pharmaceutically acceptable excipient.

44. A pharmaceutical composition comprising the compound according to claim **41**, and a pharmaceutically acceptable excipient.

45. A method for treating sepsis comprising administering a pharmaceutical composition comprising the compound according to claim **41**, and a pharmaceutically acceptable excipient.

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